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ARCHIVES OF SURGERY

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CHRONIC SUBDURAL HEMATOMA

ETIOLOGY AND TREATMENT

J. JAY KEEGAN, M.D.

OMAHA

The subject of chronic subdural hematoma has been presented in an excellent manner in recent years by several writers (Putnam and Cushing,[1] Rand,[2] Grant,[3] Holmes,[4] Brodie,[5] Sherwood,[6] Jelsma[7] and Dandy[8]), and this clinical entity is well known. The object in this paper is to contribute some observations on the source of the bleeding from the cerebral veins which cross the subdural space to enter the superior longitudinal sinus, and to add the reports of five cases in which drainage through a trephine opening was used in treatment.

The primary etiologic factor of chronic subdural hematoma is now generally recognized to be trauma to the head and the source of the bleeding, venous. The character of the injury to the head, however, is often so mild as to escape even the notice of the patient, particularly since symptoms of compression of the brain do not appear for several weeks or months after the injury. These peculiarities have clouded the picture and have led to various interpretations of the exact source and mechanism of the slow or recurrent accumulation of blood.

There also has been considerable confusion in the differentiation of traumatic chronic subdural hematoma from the nontraumatic pachymeningitis interna hemorrhagica which Virchow[9] first named in 1857

From the Division of Neurologic Surgery, University of Nebraska College of Medicine.

1. Putnam, T. J., and Cushing, H.: Chronic Subdural Hematoma, Arch. Surg. **11**:329 (Sept.) 1925.

2. Rand, C. W.: Chronic Subdural Hematoma; Report of 7 Cases, Arch. Surg. **14**:1136 (June) 1927.

3. Grant, F. C.: Chronic Subdural Hematoma, Ann. Surg. **86**:485 (Oct.) 1927.

4. Holmes, W. H.: Chronic Subdural Hemorrhage, Arch. Neurol. & Psychiat. **20**:162 (July) 1928.

5. Brodie, F.: Delayed Subdural Hemorrhage, Canad. M. A. J. **20**:273 (March) 1929.

6. Sherwood, D.: Chronic Subdural Hematoma in Infants, Am. J. Dis. Child. **39**:980 (May) 1930.

7. Jelsma, F.: Chronic Subdural Hematoma, Arch. Surg. **21**:128 (July) 1930.

8. Dandy, W. E.: Subdural Hematoma, in Lewis, Dean: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, 1932, vol. 12, p. 295.

9. Virchow, R.: Haematoma durae matris, Verhandl. d. Phys.-med. Gesellsch. Würzburg **7**:134, 1857.

and interpreted as being of inflammatory origin. He described a progressive lesion, most commonly found in asylum material and associated with cerebral atrophy, in which the formation of a very vascular subdural membrane was apparently followed by ecchymoses and subdural hemorrhage. This membrane varied in thickness, but typically measured a few millimeters and showed lamellations of blood clot on its inner surface in the more chronic cases. Virchow did not present comparative studies of traumatic subdural hematoma, which he recognized chiefly in the new-born, but thought that it was unlikely for a primary hemorrhage to produce the pathologic condition described by him.

This concept of the spontaneous inflammatory origin of such senile hemorrhagic subdural membranes gained wide acceptance and still serves to differentiate pachymeningitis interna hemorrhagica from traumatic chronic subdural hematoma (Dandy [8]). A comparative study of the two membranes was made by Putnam and Cushing,[1] who described an essentially vascular type and a reactive type of membrane in which "the gross appearance of these two forms is practically identical and the microscopic pictures so similar that they are easily confused." The chief histologic difference was the presence of large mesothelial-lined spaces in the traumatic membrane and of larger thin-walled blood vessels in the spontaneous membrane.

The recognition of trauma as a cause of chronic subdural hematoma dates back to early reports (Schuberg [10]), although its significance was often overlooked owing to delayed symptoms, and traumatic cases undoubtedly were included in descriptions of the spontaneous form. Brion,[11] Bowen,[12] Kasemeyer,[13] and Henschen [14] made notable contributions to the incidence and symptoms of traumatic subdural hemorrhage. A number of writers, (Baillarger,[15] Hewitt,[16] Sperling,[17] Hue-

10. Schuberg, W.: Das Haemtaoma durae matris bei Erwachsenen, Virchows Arch. f. path. Anat. **16**:464, 1859.

11. Brion, W.: Die operative Behandlung der intraduralen Blutungen traumatischen Ursprungs, Inaug. Diss., Strassburg, 1896.

12. Bowen, W. H.: Traumatic Subdural Haemorrhage, Guy's Hosp. Rep. **59**: 21, 1905.

13. Kasemeyer, E.: Ueber post-traumatische Pachymeningitis unter dem Biede der post-traumatischen Neurose und über deren unfallgerichtliche Bedeutung, Friedrich's Bl. f. gerichtl. Med. **62**:293, 339, 401, 1911.

14. Henschen, K.: Diagnostik und Operation der traumatischen subduralen Blutung, Arch. f. klin. Chir. **99**:67, 1912.

15. Baillarger, M.: Du siège de quelque hémorrhagies meningées, Thèse de Paris, 1837.

16. Hewitt, P.: On Extravasations of Blood into the Cavity of the Arachnoid, Tr. Med.-Chir. Soc. London **28**:45, 1845.

17. Sperling, H.: Ueber Pachymeningitis haemorrhagica interna, Inaug. Diss., Königsberg, 1872.

genin,[18] Wiglesworth [19] and Robertson [20]) questioned the primary inflammatory origin of the membrane in the spontaneous form and believed that it was the result of primary extravasation of blood into the subdural space. The cause of this bleeding was variously attributed to venous congestion, "dry-cupping" from cerebral atrophy, degenerated blood vessels and various systemic conditions or diseases of the blood. The source of the bleeding in traumatic subdural hematoma was thought to be torn meningeal vessels, supplemented by later bleeding from the lining membrane, to account for its chronic and recurrent course.

A most illuminating paper on the subject of traumatic subdural hematoma and its relation to pachymeningitis hemorrhagica by Trotter [21] appeared in 1914, which, as stated by Cushing,[1] almost had escaped attention during the period of the war. And even in this comprehensive paper by Putnam and Cushing,[1] it does not seem that enough attention was given to Trotter's [21] statements concerning the source of the hemorrhage. Since these statements can hardly be improved on, and apply particularly to case 1 of this report, it may be permissible to quote at length:

> It is nearly certain that the cerebral veins passing from the brain to the tributaries of the superior longitudinal sinus are always the source of the blood. They are short trunks passing direct from brain to dura nearly at right angles to each. Such a vein has its cranial end firmly fixed by the rigid dura, while its cerebral end is attached to the comparatively movable hemisphere. Between these two points the vein passes directly, with no tortuosity to allow for possible movement of the brain. The morbid anatomy of contusion by contre-coup shows that considerable movement of the brain is possible within the skull as the result of external violence.
>
> It is, however, characteristic of chronic subdural hemorrhage that the history of injury which has preceded the development of symptoms is usually not a striking feature of the case, and may be withheld unless specifically inquired for. Severe violence is not the kind of injury we should expect to produce the required lesion, viz., the uncomplicated rupture of one or two delicate veins. Such a trauma would be liable to complicate the condition with gross laceration or contusion of the brain, and produce conditions antagonistic to the slow or intermittent oozing required. On the other hand, comparatively slight violence favourably directed to produce an adequate displacement of the brain and nothing else, would give just the necessary conditions. It is obvious that the falx protects the brain from transverse displacement at the very place where it is most necessary to avoid displacement; at the same time, anteroposterior movement is not equally guarded against, and there can

18. Huegenin, O.: Inflammation of the Dura Mater, in von Ziemssen, Hugo Wilhelm: Cyclopedia of Practice of Medicine, American Translation, New York, W. Wood & Co., 1877, vol. 12, p. 386.

19. Wiglesworth, J.: Remarks on the Pathology of the So-Called Pachymeningitis Interna Haemorrhagica, Brain **15**:431, 1892.

20. Robertson, G. M.: The Formation of Subdural Membranes, or Pachymeningitis Haemorrhagica, J. Ment. Sc. **39**:203, 1893.

21. Trotter, W.: Chronic Subdural Hemorrhage of Traumatic Origin and Its Relation to Pachymeningitis Haemorrhagica Interna, Brit. J. Surg. **2**:271, 1914.

be little doubt that a sharp blow on the front or back of the head can comparatively easily produce a good deal of dislocation of the hemispheres, which of course would be equal on the two sides. It is interesting to notice that in all of my cases the violence had been quite moderate—in one of them extremely so,—that in three there was good reason to believe the blow had been on the front or back of the skull, and that in two the hemorrhage was bilateral.

I can amplify this conception of the source and mechanism of the bleeding in chronic subdural hematoma only by the report of a clinical case in which intermittent bleeding from an opening in the superior longitudinal sinus actually was seen during an operation two and one-half months after the primary injury of the head.

CASE 1.—*History.*—H. P. S., a man, aged 29, entered the Nebraska Methodist Hospital, on April 19, 1928. He was referred by Dr. G. A. Young, with a diagnosis of chronic subdural hematoma. The patient had been in an automobile accident about Feb. 1, 1928, and had sustained severe lacerations of the right frontotemporal part of the scalp; but there had been no loss of consciousness, vomiting or other recognized injury, and he returned promptly to work. One week or ten days later he began to have headache and pain in his right ear, which discharged purulent material. These symptoms continued for about a week and then disappeared, except for occasional headache, on account of which he did not work. About April 1, 1928, there was a severe headache for ten days, associated with pain in the right hip and thigh. This disappeared, and on April 15, 1928, there occurred a short interval when the right hand seemed weak and useless, and he was unable to speak the words he wished to use. This was accompanied by a severe headache and projectile vomiting. These same symptoms recurred on the following day and continued for a longer time.

Examination.—Neurologic examination on April 19, 1928, showed that the cranial nerves were normal except for a slightly diminished left olfactory sense. The upper extremities were normal, the abdominal and cremasteric reflexes active and the lower extremities normal. A spinal puncture showed a pressure of 24 mm. of mercury with jugular compression response, a colorless fluid, 10 cells, a normal amount of protein, a negative Wassermann test and a normal colloidal gold curve. A preoperative diagnosis of a left parietal tumor, suspected to be chronic subdural hematoma, was made.

Operation.—On April 23, an exploratory trephine in the left parietal region was done with the patient under local anesthesia. A dark, slightly adherent membrane was found beneath the dura, with no pulsation. Needle aspiration withdrew very dark blood which did not clot readily on standing. The membrane was opened; a large quantity of old blood escaped, and the cavity was irrigated with physiologic solution of sodium chloride until it returned clear. A few small clots came out. The cavity was seen to extend chiefly anteroposteriorly and medially. A rubber tissue drain was placed in the opening to permit gradual restoration of the markedly compressed cerebral hemisphere.

Course.—The patient was much improved for twenty-four hours following this operation, but pain in his head recurred the following afternoon, with restlessness, stupor and a convulsion at 3:30 a. m., on April 25. A discharge of fresh blood appeared on the head dressings, and a diagnosis of recurrent hemorrhage was made. He was taken to the operating room, and a left parietal bone flap was turned down. A similar dural flap was made, leaving the cyst wall intact, except

at the previous opening, which was plugged with blood clot. On the incision of the cyst a considerable amount of liquid blood and air escaped. The large cavity was washed out with physiologic solution of sodium chloride and a good view was obtained of its interior, which extended the full length of the skull and had compressed the cerebral hemisphere fully 3 cm. At first the wall appeared to contain no bleeding point, but when the patient began to strain from vomiting, dark blood was seen to escape intermittently from a place well forward on the superior longitudinal sinus, beneath the glabella. During a period of one half hour this place was watched, and an attempt was made to close the opening with a piece of muscle. Bleeding occurred only when the patient strained and not after the muscle was applied. The opening was a considerable distance forward and was reached with difficulty from the parietal opening. A frontal bone flap was desired for better exposure, but since no more bleeding occurred and the patient's condition from loss of blood and operative shock was not good, further work did not seem advisable. A rubber tissue drain was placed well forward over the hemisphere, and the bone flap was replaced. The patient was improved in reaction for a few hours, but fresh blood again appeared on the dressings, and he became comatose, indicating further bleeding. He was taken to the operating room, and a triangular piece of bone was elevated in the left frontal region, directly over the bleeding point. Blood clot and active intermittent bleeding were found again coming from the superior longitudinal sinus, where an anterior cerebral vein must have been torn out at the time of the injury. This opening was closed by silver clips and electrosurgical coagulation. The cerebral hemisphere this time appeared much larger, indicating more active replacement of tissue fluid. It was hoped that this final closure of the venous opening would result in recovery, but the patient did not regain consciousness and died the following day after gradually rising temperature and pulse and respiratory rates not relieved by dehydration therapy. Postmortem examination was not permitted.

This case presents the unique observation of a persisting opening in the superior longitudinal sinus which evidently was the source of the large subdural hematoma found at operation, two and one-half months after a mild injury of the head. It confirms the generally accepted concept of the origin of this lesion from ruptured cerebral veins as they cross to enter the sinus, and explains the slow and intermittent accumulation of blood which has seemed necessary to produce the clinical symptoms. The unfortunate outcome was due to the unusual persistence of this opening, leading to postoperative hemorrhage, to the inaccessible location of the opening from a parietal bone flap and to postoperative edema of the brain.

The latent interval, with gradual or intermittent accumulation of blood or serum in subdural hematoma, has long been a puzzling feature of the condition. Most writers, following Virchow's [9] lead, have assumed repeated ruptures of thin-walled blood vessels in the lining membrane. Gardner [22] recently has offered experimental evidence that cerebrospinal fluid is drawn into the sac through the arachnoid by

22. Gardner, W. J.: Traumatic Subdural Hematoma; with Particular Reference to the Latent Interval, Arch. Neurol. & Psychiat. **27**:847 (April) 1932.

osmosis. Both of these factors may play a part, but the demonstrated intermittent bleeding from the superior longitudinal sinus in the preceding case would seem to be a more logical explanation to account for the major portion of the accumulated contents of the sac.

A few added deductions in support of Trotter's [21] conception of the origin of chronic subdural hematoma might be presented. Our present knowledge of posttraumatic edema of the brain indicates that injuries of the head severe enough to produce even transient unconsciousness are liable to be followed by appreciable signs of edema of the brain. This tends to compress the subarachnoid and subdural spaces by swelling of the brain and would favor closure of any torn veins long enough for a firm thrombus to form and prevent extensive or recurrent bleeding. The absence of edema of the brain following the mild injury of the head in which simple displacement of the brain occurs, as in the frontal or occipital bump, might permit subdural venous bleeding. The added factors of normal activity and straining following the injury to the head and the rigid wall of the opening in the superior longitudinal sinus would favor continued intermittent bleeding.

Following this reasoning a little farther offers an explanation of the observed frequency of chronic subdural hematoma in conditions of cerebral atrophy (Bowen [12]). It is a common postmortem observation in such cases, and now frequently seen in encephalograms (fig. 1), that the retracted cerebral hemispheres appear suspended at their medial borders by the venous connections to the superior longitudinal sinus. This condition, combined with the mild blows on the head which these patients commonly suffer or the venous congestion from straining, coughing or convulsions, would favor rupture of these venous connections and permit free subdural hemorrhage. Trotter [21] likewise emphasized these factors as a possible explanation of spontaneous subdural hemorrhage in conditions of cerebral atrophy.

It is not contended on the basis of this single case that all subdural hematomas arise from bleeding from the superior longitudinal sinus. Many other sources are possible, one of which was excellently portrayed in Rand's [2] paper as being a ruptured large cerebral vein over the convexity of the hemisphere. Middle meningeal subdural hemorrhage may persist without operation for many weeks, as was suspected in case 4 of this report. A cerebral aneurysm may rupture at the base of the brain into the subdural space and produce a large and rapidly fatal subdural hematoma, as was reported by Bennett and myself.[23] Birth injury may give rise to subdural hemorrhage over the tentorium. But rarely would any of these traumas produce the clinical and pathologic condition of chronic subdural hematoma.

23. Keegan, J. J., and Bennett, A. E.: Cerebral Aneurysm and Cortical Herniation, Arch. Neurol. & Psychiat. **26**:36 (July) 1931.

The treatment of chronic subdural hematoma has varied greatly, often depending on the neurosurgical qualifications of the operator or the serious condition of the patient which did not permit an extensive operation. However, guided by Virchow's [9] conception of the etiologic significance of the lining membrane and Putnam and Cushing's [1] recommendation, an osteoplastic flap and thorough removal of the membrane generally have been advocated (Rand [2] Grant [3] Jelsma [7] and Dandy [8]). Fortunately not all patients have been subjected to this major procedure, and an increasing number of satisfactory recoveries have been reported after simple evacuation through a trephine opening.

Fig. 1.—Encephalogram of a patient with chronic epilepsy, showing cerebral atrophy and suspension of the cerebral hemispheres by venous connections to the superior longitudinal sinus.

Two recent critical surveys of methods of treatment by Fleming and Jones [24] and McKenzie [25] definitely have favored the simpler procedure and called attention to the similar recommendation of Trotter [21] in 1914. I am in agreement with this conservative method of treatment and have applied it in my cases with reasonable success. The problem, however, is not quite so simple that a fixed rule can be applied to all

24. Fleming, H. W., and Jones, O. W., Jr.: Chronic Subdural Hematoma, Surg., Gynec. & Obst. **54**:81 (Jan.) 1932.

25. McKenzie, Kenneth G.: A Surgical and Clinical Study of Nine Cases of Chronic Subdural Haematoma, Canad. M. A. J. **26**:534 (May) 1932.

cases. Each must be considered in the light of both preoperative and postoperative findings; the presence or absence of organization in the hematoma which may favor delayed resolution and epilepsy; the size and duration of the lesion which may caused delayed obliteration of the cavity or predispose to postoperative edema of the brain; the danger of recurrent hemorrhage as in case 1, and the persistence of a low grade pressure syndrome which may require decompression for relief as in case 2 (fig. 2).

From my limited experience and deduction from the literature, I should favor the following procedure in treatment. In all cases of sus-

Fig. 2 (case 2).—Encephalogram taken in a case of right subdural hematoma occurring six weeks after trephine drainage.

pected chronic subdural hematoma, exploration should be made through a small lateral frontal or parietal trephine, which can be made a part of a large frontoparietal bone flap if necessary. Simple evacuation by suction and irrigation with physiologic sodium chloride with rubber tissue drainage for forty-eight hours should be the preliminary procedure, unless dense organization of the clot is found. Moderate dehydration therapy by limitation of fluid, magnesium sulphate catharsis or intravenous injection of a hypertonic solution of dextrose should follow the operation for a few days to counteract the tendency toward edema of the brain. Most patients probably will recover satisfactorily under this conservative regimen. A bone flap is indicated to remove an organized thrombus or to find the source of a recurrent hemorrhage, but not for

removal of the ordinary thin protective membrane surrounding the hematoma. This membrane will disappear within a few months, as in a case reported by Horrax and quoted in McKenzie's [25] paper, or become insignificant as in case 2 of this report (fig. 3). Drainage for forty-eight hours would seem to be indicated both to allow the escape of some retained blood and to permit the escape of fluid and air as the markedly compressed brain gradually is restored to normal volume. A subtemporal decompression might well be made a part of the original operation to allow for some unavoidable postoperative pressure from edema of the brain, or to relieve a low grade chronic pressure syndrome from arachnoiditis as in case 2. The possibility or even the probability of a bilateral hematoma, as emphasized by Trotter [21] and by Fleming and Jones,[24] always should be kept in mind and bilateral trephine exploration done on the slightest evidence. Double trephine openings as advocated by Fleming and Jones [24] probably are not necessary, although they add little hazard to the operation and perhaps insure more complete evacuation of the hematoma.

SUMMARY

The primary etiology of chronic subdural hematoma is mild trauma to the head, and the source of the bleeding is torn veins which connect the cerebral hemispheres with the superior longitudinal sinus.

Edema of the brain following severe injury of the head compresses torn veins, favors clotting and prevents large subdural accumulation of blood.

The latent period and intermittent bleeding are demonstrated by the case reported to be due to a persisting opening in the superior longitudinal sinus.

Cerebral atrophy causes suspension of the cerebral hemispheres by their venous connections to the superior longitudinal sinus and makes these patients more susceptible to subdural hemorrhage.

Trephine exploration and drainage should be used in treatment, unless specific indications call for more radical surgical procedures.

CASE 2.—*History.*—P. R., a man, aged 24, entered the Jennie Edmundson Hospital, Council Bluffs, Ia., on Nov. 9, 1931. He was referred by Dr. S. D. Maiden, with a diagnosis of intracranial pressure. This patient was in an automobile collision on July 19, 1931. He suffered no serious injury, was not aware of any injury of the head, and did not lose consciousness. Two days later he began to have frontal and temporal headache, which persisted and gradually became worse. On September 1, rather severe intermittent pain in the right frontal area developed, for which he consulted a specialist in diseases of the nose and throat. Cocainization of the right nares relieved the pain. There was no choked disk at this time. The pain recurred, and the right maxillary antrum was drained on September 14, with some relief. He returned in a few days with a history of an attack of transient weakness or dead feeling in his left arm. Examination of the fundus showed a

papilledema of 4 diopters with hemorrhages. The visual fields showed some color restriction but no segment defect. The spinal fluid pressure was 18 mm. of mercury; there were 10 cells and the fluid was colorless.

Examination.—Neurologic examination, on September 21, showed a questionable weakness of the left side of the face and of the tongue; otherwise the reactions to motor, sensory, reflex and coordination tests were normal. The tendon reflexes were slightly sluggish; the abdominal and cremasteric reflexes, active. The patient appeared apathetic and yawned frequently, although he was responsive and rational. There were: a low grade fever, a leukocyte count of 17,000, with 88 per cent polymorphonuclears, a pulse rate of 74 and a blood pressure of 130 systolic and 70 diastolic. There was no history of suppuration of the ear or sinus trouble, but a peritonsillar abscess had been lanced in July, 1930, and the patient had not felt entirely well since. With this history suggestive of infection and the patient's positive statement that he had not injured or struck his head in the automobile accident, the preoperative diagnosis favored right frontal abscess rather than hematoma. An exploratory trephination was done in the right lateral frontal region on September 22, and a dark bluish membrane, characteristic of chronic subdural hematoma was encountered. Two or 3 ounces (56 to 85 Gm.) of dark liquid blood was removed by suction, and a rubber tissue drain was left inserted in the cavity, one drain extending into the temporal fossa where evacuation did not seem complete. The drains were removed after forty-eight hours; there was moderate drainage of old blood during the first twenty-four hours.

The patient promptly improved in alertness and was relieved of pain, although for a few days he complained of an occasional sensation of numbness in his left hand. Headache occurred on October 14, and vision seemed slightly blurred. A choked disk of 4 diopters persisted. The cisternal cerebrospinal fluid pressure was 22 mm. of mercury; 30 cc. of fluid was removed, the pressure being reduced to 8 mm. The patient felt relieved after this drainage, but symptoms recurred in about a week and cisternal pressure of 18 mm. was found; 25 cc. of fluid was removed on October 21. The papilledema had subsided to 2 diopters, and vision was better. On Oct. 28, cisternal pressure was 12 mm., and 25 cc. of fluid was removed. The pressure seemed to be subsiding, but on Nov. 2, it rose to 20 mm. again, and the patient complained of frontal headache and pain in his eyes. He did not feel well and had not regained normal physical and mental reactions.

Second Admission.—He was admitted to the Nebraska Methodist Hospital on November 9, for an encephalogram, to determine the presence of a suspected residual hematoma. Before the injection of air a needle was inserted through the old trephine opening, and no fluid was obtained. The encephalogram showed a partial obliteration of the subarachnoid spaces over the right hemisphere and slight displacement of the ventricles to the left, with asymmetrical dilatation of the ventricles, more pronounced on the left. The findings indicated an obliterative pressure lesion over the lateral surface of the right hemisphere. A needle was inserted through the old trephine opening in search of old blood, but nothing was found. From this it was interpreted that there probably was a walled-off hematoma in the right temporal fossa where evacuation was imperfect at operation.

The patient was allowed to go home, and felt considerably improved for two weeks following the encephalogram. Cisternal pressure was found to be normal on November 18, but the patient returned to the hospital on November 25, with headache and pain in his eyes again and a pressure of 18 mm. of mercury. Symptoms and an increased intracranial pressure of 14 mm. persisted until December 2, and operation was advised.

Operation and Course.—At this operation, Dec. 3, 1931, preparation was made to turn down a large bone flap in the right frontoparietal region. A preliminary temporal trephine with the patient under local anesthesia was done, and the dura was opened. A thin subdural membrane was found, but no blood. The opening in the temporal bone was enlarged and the dura opened widely for decompression. The subdural membrane separated easily from the dura and was detached over a wide area by traction. Exploration with a spatula beneath the temporal lobe did not reveal blood. The exposed cortex had a gray, translucent, wet appearance, with some clouding of the arachnoid, interpreted as a definite local arachnoiditis and edema of the brain. The wound was closed, leaving a subtemporal decompression.

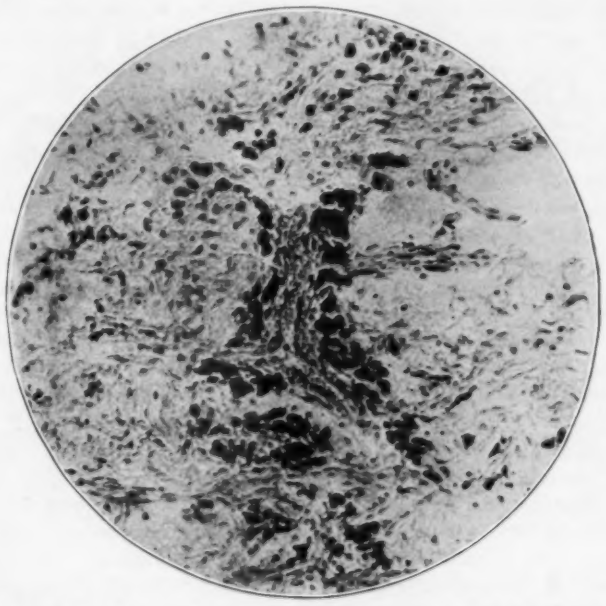

Fig. 3 (case 2).—Photomicrograph, low power, of the membrane of the subdural hematoma three and one half months after evacuation of the blood through a trephine.

The former right frontal trephine was reopened and no subdural fluid was found, which confirmed the negative results of the needle puncture.

The patient made an uncomplicated recovery, and left the hospital on December 10. He was given 100 cc. of a 50 per cent solution of dextrose intravenously on the first postoperative day. There was moderate bulging over the decompression when he left, but this had entirely subsided when he was next seen, on Jan. 27, 1932. At this time he had no complaint, had gained in weight, strength and alertness, and felt entirely well. He has remained well.

Microscopic section of the subdural membrane (fig. 3) showed hyalinized connective tissue, a few thin-walled blood vessels and some hemosiderin pigment.

Comment.—This case illustrates the significance of anteroposterior displacement of the brain in the causation of chronic subdural hema-

toma, in that the sudden stopping of the car, with powerful bracing on the steering wheel, and no recognized injury of the head, gave rise to the condition. It also illustrates the successful evacuaton of the hematoma by trephine and drainage, but with persistence of low grade pressure signs from residual local arachnoiditis and cerebral edema. This was relieved promptly by subtemporal decompression, which exposed the apparently insignificant loose remnant of the cyst wall seventy-one days after trephine drainage.

CASE 3.—*History.*—O. M. N., a man, aged 46, entered the Nebraska Methodist Hospital on April 23, 1923. He was referred by Dr. G. A. Young, with a diagnosis of chronic subdural hematoma. The patient entered the hospital with the complaint of headache, vomiting, inability to think and remember, and weakness. About Dec. 11, 1922, he fell from a load of hay and received a blow on his forehead, and a fracture of the left clavicle occurred. He was not unconscious, and drove his team to the barn. He had a headache following the accident, which soon disappeared, and he thought no more of the injury to the head. As soon as the clavicle had mended sufficiently, he resumed work and his health was normal. About Feb. 20, 1923, a sudden headache developed accompanied by vomiting, without nausea. The headache lasted a day or two; it was located indefinitely in the top of his head. He then appeared well again. During the following weeks, however, he had several similar attacks of headache lasting two or three days. During the two weeks preceding admission to the hospital his condition had become much worse and the headache more frequent and persistent; he had not been able to think clearly. During the past few days he had been very slow to respond; he appeared confused and at times unconscious.

Examination.—The patient lay in a semiconscious state. He responded very slowly and inaccurately. The left pupil was larger than the right; the fundus showed no elevation, and no other evident abnormality of the cranial nerves was present, although the patient's sluggish mental reaction prevented accurate tests of smell and taste. There was slight rigidity of the neck, and the Kernig sign was negative. Muscle power, reaction to pain, knee jerks and biceps tendon reaction appeared diminished on the left side. The Babinski reflex was negative. Spinal pressure on April 24 was 25 mm. of mercury; the fluid was clear and colorless, with 2 cells. The Wassermann reaction and the colloidal gold curve were negative. On April 25, the patient was more stuporous; the left abdominal reflex was absent, and the Babinski reflex and ankle clonus on the left were positive. The temperature and respiratory rate were normal; the pulse rate, from 50 to 60 a minute, and the blood pressure 95 systolic and 65 diastolic. Roentgenograms of the head were negative.

First Operation.—The findings suggested a tumor of the right frontal lobe. Examination of the fundus on April 25 showed an elevation of from 2 to 3 diopters in the left disk; the right disk was normal. The respiration had become Cheyne-Stokes in character; the pulse rate, 45, the stupor more profound. An intravenous injection of 200 cc. of buffered 15 per cent solution of sodium chloride was given and a right subtemporal decompression performed, with the patient under local anesthesia, as an emergency measure. There was no intracranial pressure during the operation, and no evident pathologic process was found in the right temporal region of the brain.

There was not much change following the operation, although consciousness was slightly improved. The left optic disk was normal on May 6. There was moderate bulging over the decompression, with little tension. On May 12, the mental condition was considerably improved, and absence of smell in the left nostril was observed. Replacement of ventricular fluid by 40 cc. of air was done through the decompression opening on May 12. The ventriculogram showed a markedly dilated right lateral ventricle with no deformity in the frontal region. The third ventricle also appeared markedly dilated and displaced to the right. No air was found in the left lateral ventricle. The interpretation was that there was a tumor in the left frontal region instead of the right as previously suspected. It was thought probably to be an inoperable glioma, owing to the rapid progression of symptoms, without marked intracranial pressure, and its location was thought to be the left frontal lobe. Chronic subdural hematoma was not thought of, although a history of injury of the head was obtained, because at that time this clinical condition was not well known.

Second Operation and Course.—A left frontal osteoplastic flap was turned down on May 17, with the patient under ethylene anesthesia. A large subdural hematoma was found over the left frontal lobe, filled with dark liquid blood and extending posteriorly as a thinner layer beyond the central fissure. The outer wall of the cyst was removed anteriorly, and a considerable amount of fibrinous clot was removed by sponging and irrigation. No attempt was made to remove the entire lining. The membrane was thin over the arachnoid, so that the flattened cerebral convolutions and fissures could be seen through it. A drain was placed in the cavity and another outside of the closed dura at the posterior angle of the wound.

There was considerable drainage of blood from the wound during the first twenty-four hours. The drains were removed on the second day, with no further evidence of bleeding. The wound healed without complications. There was moderate bulging over the right decompression for several days, which had subsided on May 24.

The patient made a rapid and uncomplicated recovery. He left the hospital on May 24, the seventh postoperative day, with continued nursing care at home. He resumed normal activity in a few weeks and continued to be well until Aug. 27, 1925, when he had three convulsions over a period of twenty-four hours. He reentered the hospital on August 28, and neurologic examination at that time gave entirely negative results. Examination of the spinal fluid showed: pressure, normal; cells, 2, and protein and sugar content, normal. He was dismissed on August 30, with a diagnosis of organic epilepsy, and medical treatment was advised. He has had occasional epileptic attacks since that time, mostly of the minor type, and on this account has some disability. His general health otherwise is good.

Comment.—This case illustrates the delay in diganosis and treatment incident to imperfect knowledge of chronic subdural hematoma in 1923. Although a bone flap was turned down, the hematoma was treated essentially by evacuation and drainage. The desirability of a decompression during the period of recovery is shown by the bulging right temporal hernia which lasted several days. Recovery probably was hastened by the presence of this decompression. The appearance of epileptic attacks two years after the operation might indicate some residual scarring which could have been prevented by more radical

removal of the membrane. However, I should question whether less damage would be left by complete removal, which is not always possible or advisable.

CASE 4.—*History.*—C. N., a man, aged 57, entered the Nebraska Methodist Hospital on June 7, 1928. He was referred by Dr. C. E. Allenburger, with a diagnosis of chronic subdural hematoma.

The patient entered with the complaint of persistent right frontal headache, occasional vomiting, mental confusion and weakness. Early in April, 1928, while working in the field, he received an injury to the right side of his head. He wandered into the house about 11 a. m., apparently dazed and confused, with a severe lacerated wound in the right temporal region. The wound was sutured, and a roentgenogram was not taken. The mental confusion seemed to have disappeared by the evening of that day. He returned to work after a few days and seemed well, except for a gradually increasing right frontotemporal headache, which caused him to consult a physician on May 29. The following day he became quite weak, unable to walk, and entered a local hospital on June 2. Occasional vomiting began at this time. Mental confusion appeared on June 5, and he entered the Methodist Hospital on June 7.

Examination.—Examination showed mental dulness, difficulty in holding attention, a tendency toward jocularity, at times a mild stupor. The optic disks showed blurring of the margins and an elevation of 1 diopter; there was no defect in the visual fields, and all of the other cranial nerves were normal. There was a slight motor weakness in the left arm. The knee jerk was greater on the left than on the right; there were bilateral ankle clonus, a left plantar reflex and absence of abdominal and cremasteric reflexes. Otherwise the results of motor, sensory and coordination tests were normal, except for sluggish response. Roentgenograms of the skull were negative.

Operation and Course.—A preoperative diagnosis of chronic subdural hematoma in the right frontal area was made, and a right lateral, frontal trephine was done on July 8. A thin, partly organized old blood clot was found in the subdural space, but there was little free fluid. This wound was closed, and another trephine was done posteriorly in the right temple. An elevated line of bone in this region with quite adherent dura and obliterated middle meningeal artery suggested an old fracture and middle meningeal tear. The trephine opening was enlarged to 2 cm. in diameter, and the dura was opened crucially. At the inferior border of the opening a considerable quantity of clear fluid under pressure was released, apparently subarachnoid fluid, with the cortex visible in this region. A dark membrane covered the upper two thirds of the opening, and a trochar needle inserted into this released 2 or 3 ounces of dark brown fluid. The opening was enlarged, and a rubber tissue drain was inserted into this cavity. There was considerable drainage of blood-stained fluid during the first twenty-four hours, interpreted as partly cerebrospinal fluid. The drain was removed on the second day, with no further drainage.

The patient seemed more alert after the operation and had less headache. A spinal puncture on June 11 showed: pressure, 18 mm. of mercury; fluid, clear; cells, 8; protein, normal. He was rather restless for a few days and then became listless and drowsy. He was given active magnesium sulphate catharsis for the edema of the brain. Spinal puncture, on June 15, showed a low grade pressure, with normal fluid. A needle was inserted into the region of the hematoma on June 16, and only 8 cc. of brown fluid could be obtained, indicating satisfactory evacuation. The persistence of neurologic signs which preceded the operation, increasing stupor

with bilateral ankle clonus, and a suggestive spastic weakness of the right arm observed on June 29, suggested a bilateral hematoma. A left frontal trephine was done on June 30, and nothing was found, except an increase of subarachnoid fluid and prominence of the cortical blood vessels.

The stupor gradually increased to coma, with Cheyne-Stokes respiration, loss of pharyngeal reflexes and profuse sweating, with periods of slight remission. The pulse remained fairly good; the temperature ranged from 99 to 101 F. and the respiratory rate, from 20 to 30 a minute. On July 3, convulsive attacks developed, characterized by clonic spasm spreading from the right side of the face down the right side of the body, with conjugate deviation of the eyes to the right. These recurred for several days, and the patient's condition seemed very serious. The temperature rose to 103 F., the pulse rate, to 120, and the respiratory rate, to 40. He gradually improved, however, regained consciousness, became restless but more cooperative, and was able to be up in a chair on July 14. From this time he improved rapidly. He left the hospital July 20. He gradually recovered strength, and when seen on Sept. 11, 1928, appeared to be entirely well. He was seen again on Oct. 30, 1930, and reported ability to do a full day's work on the farm as well as before his injury.

Comment.—This case presents several puzzling features. The operative findings indicated a right middle meningeal injury, but the location of the hematoma was almost too far medial and the symptoms too slow in developing for its source to be this vessel. The persistence and increase of symptoms after drainage of the hematoma led to exploration of the left side, with negative results. Postoperative edema of the brain did not seem to explain the profound depression without pressure; cortical degeneration seemed necessary; but the patient's complete recovery would negative this theory. Perhaps a bone flap or larger decompression should have been done, since there was evidence of organization of the clot in the frontal region. I doubt, however, if he would have survived this major operation. Intravenous injections of a hypertonic solution of dextrose might have been given to advantage, although the excess of subarachnoid fluid on the left side indicated adequate dehydration by magnesium sulphate. It is possible that the patient was too much dehydrated, and that hypotonic rather than hypertonic fluids were indicated.

CASE 5.—*History.*—P. M. S., a man, aged 71, entered the Immanuel Hospital on Feb. 11, 1932. He was referred by Dr. H. A. Blackstone, with a diagnosis of chronic subdural hematoma.

The patient fell on a slippery street on Dec. 11, 1931, striking the right frontotemporal region of his head. He got up immediately after the injury and went home alone, with no symptoms except a "black eye." About two weeks later, his son noted that his left knee seemed stiff, and that he dragged the left toes in walking. The left arm became weak about two weeks later, and the weakness gradually increased to disabling left hemiplegia. He had no headache and did not vomit, and no mental disturbances appeared until Feb. 1, 1932, when he had influenza and became increasingly drowsy, with stupor and incontinence two weeks later.

Examination.—Neurologic examination, on February 16, showed: left hemiplegia of the central type; absence of the left abdominal and cremasteric reflexes; normal fundi; spinal pressure, 10 mm. of mercury; fluid, clear with a very faint yellow tint; cell count, 2; protein, 13 mg. per hundred cubic centimeters; colloidal gold curve, negative. The pulse ranged between 64 and 84; the blood pressure was 120 systolic and 80 diastolic. He was stuporous and slept with obstructed breathing.

Owing to his age and lack of intracranial pressure, a diagnosis of right lateral cerebral thrombosis was favored, although the traumatic history suggested chronic subdural hematoma. In a report on the roentgen findings, Dr. Tyler stated that there was "an area of increased density in the right lateral frontal region very suggestive of hemorrhage between the cranial vault and the brain, pushing the latter away from the skull." Definite improvement following the intravenous injection of 100 cc. of a 50 per cent solution of dextrose favored the diagnosis of chronic subdural hematoma.

Operation and Course.—An exploratory trephine in the right lateral frontal region was done on February 20, and a typical dark subdural membrane was encountered. Incision through this released an ounce or more of dark brownish liquid blood. After evacuation the blood cavity was found to extend several centimeters medially and into the temporal region. There appeared to be an inner chamber of blood which required separate opening before the pale fairly normal-appearing flattened cortex could be seen. A considerable portion of the cyst membrane was removed by dissection and traction. The wound was closed, and a small rubber tissue drain was left in place for forty-eight hours.

Following the operation there was prompt improvement in mental reaction and the disappearance of drowsiness, but there was little improvement in the paralysis. This, however, gradually improved over a period of a few months, and at the present writing the patient has resumed normal activity, with slight disability.

Comment.—This case illustrates the danger of a mistaken diagnosis of cerebral vascular disease on account of the age of the patient. The noteworthy roentgenographic report of a subdural shadow and the improvement following injection of a hypertonic solution of dextrose, with a history of trauma, led to the correct diagnosis. In this case recovery after simple trephine drainage was complete but slow. It is possible that more rapid recovery would have occurred if a larger opening had been made or a decompression done. However, the age and poor condition of the patient seemed to contraindicate a more radical surgical procedure. His ultimate recovery was satisfactory.

OSTEOCHONDRITIS OF THE HEAD OF THE FEMUR

AN EXPERIMENTAL STUDY

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The exact etiology of osteochondritis of the head of the femur [1] is still undetermined. Various theories of the cause of this disease have been advanced, the most reasonable of which may be considered under the headings of infection, trauma, embolism and maldevelopment.

The evidence in favor of infection as the etiologic agent is based on a few bacteriologic studies. Legg [2] scraped tissue from a large area of rarefaction in the neck of the femur of a patient suffering from this disease and found that staphylococci grew in cultures from the material so obtained. Kidner [3] obtained staphylococci from the granulation tissue found in necrotic areas in the metaphyseal region of the upper end of the femur in a similar case. McWhorter [4] likewise found the staphylococcus in a single case. Phemister [5] removed part of the upper femoral epiphysis after curetting the interior, and obtained no microbic growth (1921), but in a later study (1930) of two cases, he found in one streptococci in cultures of tissue removed at operation. In this case, the wound healed by primary intention, but a low grade febrile reaction persisted for two weeks. A blood culture taken during this period yielded the same organisms as those which were recovered from the bone. The histologic picture was that of necrosis of the bone accompanied by marked fibrosis and phagocytic reaction of the fixed tissues.

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1. Synonyms for osteochondritis of the head of the femur are Legg-Calvé-Perthes' disease, osteochondritis deformans juvenilis coxa and pseudocoxalgia.

2. Legg, A. T.: An Obscure Affection of the Hip Joint, Boston M. & S. J. **62**:202 (Feb. 17) 1910.

3. Kidner, F. C.: Perthes' Disease, Am. J. Orthop. Surg. **14**:339, 1916.

4. McWorther, G. L.: Operation on the Neck of the Femur Following Acute Symptoms in a Case of Osteochondritis Deformans Juvenilis Coxae, Surg., Gynec. & Obst. **38**:632, 1924.

5. Phemister, D. B.: Operation for Epiphysitis of the Head of the Femur (Perthes' Disease), Arch. Surg. **2**:221 (March) 1921; Silent Foci of Localized Osteomyelitis, J. A. M. A. **82**:1311 (April 26) 1924. Phemister, D. B.; Brunschwig, A., and Day, L.: Streptococcal Infections of the Epiphyses and Short Bones, J. A. M. A. **95**:995 (Oct. 4) 1930.

However, in a number of patients subjected to exploratory operation by other workers, the cultures failed to show bacterial growth.

As a definite history of trauma is often obtained in osteochondritis it is difficult to discount this factor entirely. Not infrequently changes simulating osteochondritis develop after closed manipulation in congenital dislocation of the hip. It has been suggested that such trauma may injure the vessels supplying the femoral epiphysis and that the circulatory disturbance produced thereby may cause atrophy of the bone with collapse of the head. In this connection it may be well to recall that the head of the femur receives its main blood supply from the vessels of that portion of the capsule which is reflected upward along the neck to the chondro-osseous margins. A rich anastomosis of these vessels encircles the entire neck of the femur with the largest vessels situated posteriorly and superiorly. In young persons the ligamentum teres contains blood vessels which aid in the nutrition of the head. Leriche and Policard [6] suggested an explanation of osteochondritis on the basis of traumatic vasomotor changes. They found that rarefaction of bone is the result of increased circulation. Bentzon,[7] whose investigations support this idea, believes that the arteries which supply the femoral head are so arranged that they are exposed to mild lesions of pressure and stretching, especially in young persons in whom trauma may cause a bending of the cartilaginous part of the epiphysis without producing a real epiphyseolysis. He stated that since the arteries are exposed to moderate traumatisms, it is possible that the vasomotor nerves in the adventitia may be damaged in such a way that they become blocked, with the result that an active hyperemia of the epiphyseal body occurs. By injections of alcohol around the arteries of the upper epiphysis of the femur in young rabbits he produced coxa plana in several instances, and histologic examination of the femoral heads showed a picture quite characteristic of that condition.

Axhausen [8] suggested that Legg-Calvé-Perthes' disease, Kienbock's disease, Köhler's disease and similar lesions might represent the results of a vascular occlusion caused by an embolus of tubercle bacilli or pyogenic organisms. He believes that bacteria may lodge in one or more of the smaller vessels, where they are destroyed by the local protective

6. Leriche, R., and Policard, A.: Normal and Pathological Physiology of Bones, St. Louis, C. V. Mosby Company, 1928, p. 214.

7. Bentzon, P. G. K.: A New Theory About the Pathogenesis of Coxa Plana and Other Manifestations of "Local Dyschondroplasia," Brit. J. Radiol. **31**:439, 1926.

8. Axhausen, G.: Nicht Malacie, sondern Nekrose des Os Lunatum Carpi, Arch. f. klin. Chir. **129**:26, 1924; Ueber anämische Infarkte am Knochensystem und ihre Bedeutung für die Lehre von den primären Epiphyseonekrosen, ibid. **151**: 72, 1928.

forces with a sterile embolic necrosis as the end-result. In support of this contention it can be stated that tubercle bacilli have been found in several cases which have shown a clinical course similar to that of Legg-Calvé-Perthes' disease.

Calot [9] and Mürk Jansen [10] offer to explain the disease on the basis of developmental anomalies. The former believes that osteochondritis of the femoral head is a condition of arrested development of the hip joint, with a tendency to congenital subluxation or dislocation. An imperfect contact of the head in the acetabulum brings about a condition of mechanical instability which results in flattening and irregularity of the head. Mürk Jansen stated that in these cases the acetabula are abnormally flat (ischium varum), and the head changes its shape gradually because of the deranged mechanical conditions.

Because of the limited amount of material available for microscopic examination, the histopathology of osteochondritis of the head of the femur has not been investigated thoroughly. Nevertheless, the essential features of the anatomic changes have been well described in a few pathologic studies made by German workers (Perthes, Axhausen, Riedel, Heitzmann, Konjetzney, Brandt and Klages). The earliest and most striking change consists in necrosis of the bony trabeculae of the femoral head and of the bone marrow, resulting occasionally, when extensive, in compression fracture of the head. This necrosis is followed immediately by regenerative activities on the part of the fibroblasts. Beginning as a zone of granulation tissue surrounding the necrotic area, the fibrous tissue tends to reorganize the areas of necrosis. Subsequently, there is not only diffuse fibrosis of the bone marrow, but also formation of new bone and cartilage as the result of the metaplasia of the fibroblasts or the increased activities of the chondroblasts and osteoblasts. In the granulation tissue degenerative changes may develop. These consist especially of hemorrhage, edema and finally the formation of small cysts. Additional changes also occur at the epiphyseal line and in the joint cartilage. The epiphyseal line may be broken into irregular islands of cartilage, with the result that the vascular channels between the medullary bone of the head and neck become anastomosed. The hyaline matrix of the joint cartilage may become edematous or fibrillar, and the cartilage cells may either absorb stain poorly or appear greatly shrunken and atrophied.

That one or more of the causal factors previously suggested plays a part in the etiology of osteochondritis of the hip seems possible. It is

9. Calot, F., and Collen, H.: L'ostéochondrite de la hanche, Presse méd. **30**: 35 (Jan. 14) 1922.

10. Jansen, Mürk: Flattened Hip Socket and Its Sequelae, J. Bone & Joint Surg. **5**:528, 1923.

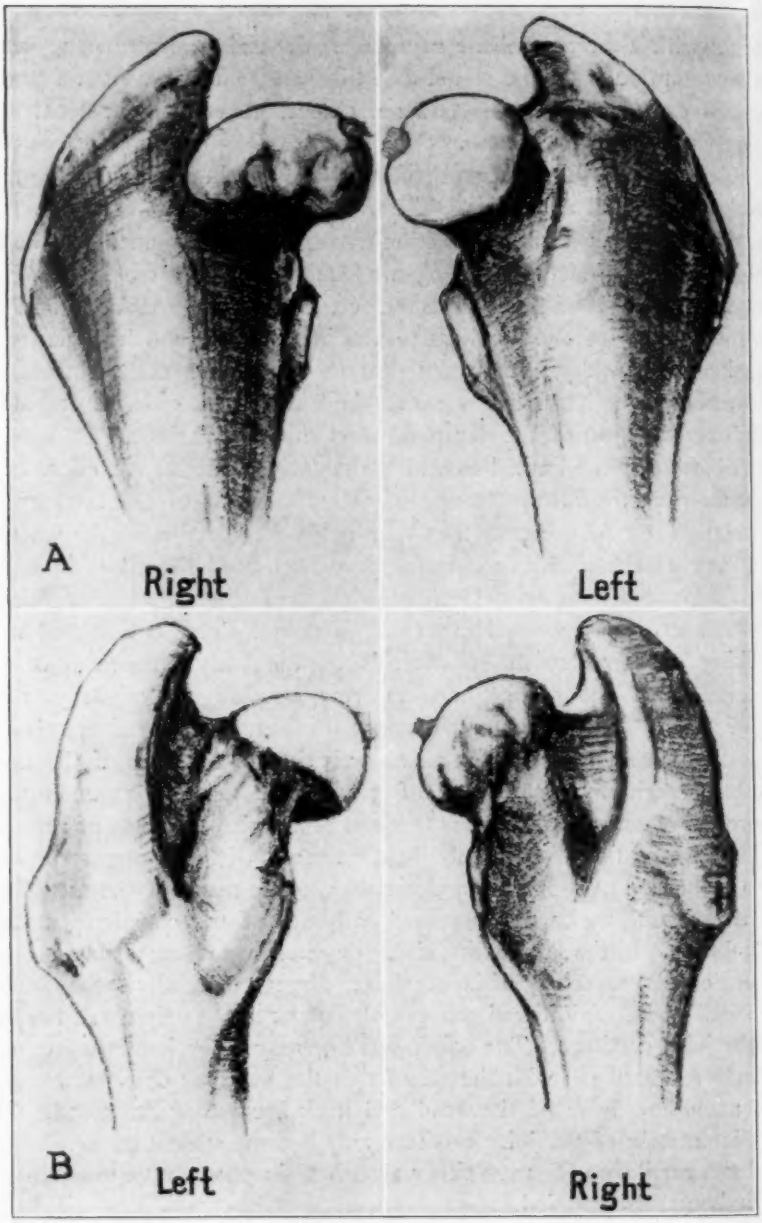

Fig. 1.—*A*, drawings (anterior view in case 365) showing the early roughening and flattening of the right femoral head. The operation, which was performed three months previously, included ligation of the round ligament along with stripping of the periosteum from the neck. Note that most of the changes of the head are in the portion nearest the epiphyseal cartilage plate. The normal left femoral head is shown for comparison. *B*, posterior view of the same specimens.

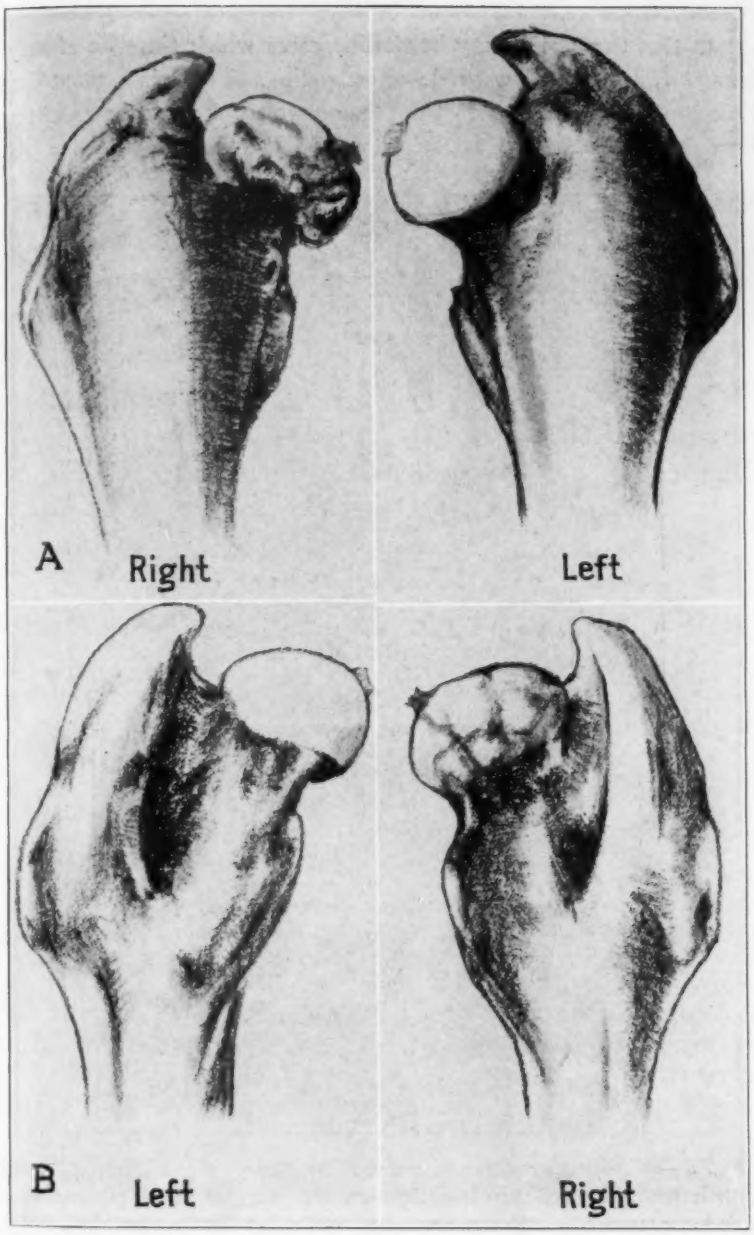

Fig. 2.—*A*, drawing of the autopsy specimen in case 399 removed four months after ligation of the round ligament and stripping of the periosteum from the neck (right side). Note that the changes are more advanced than those in figure 1, and include roughening and flattening of the entire head. The normal left femoral head is shown for comparison. *B*, posterior views of the same specimens.

certain that there are many borderline cases which simulate closely the changes following a low grade osteomyelitis. There is a great deal of clinical evidence in support of the traumatic theory. After an extensive survey of the literature, it seemed to us that the cause of the disease

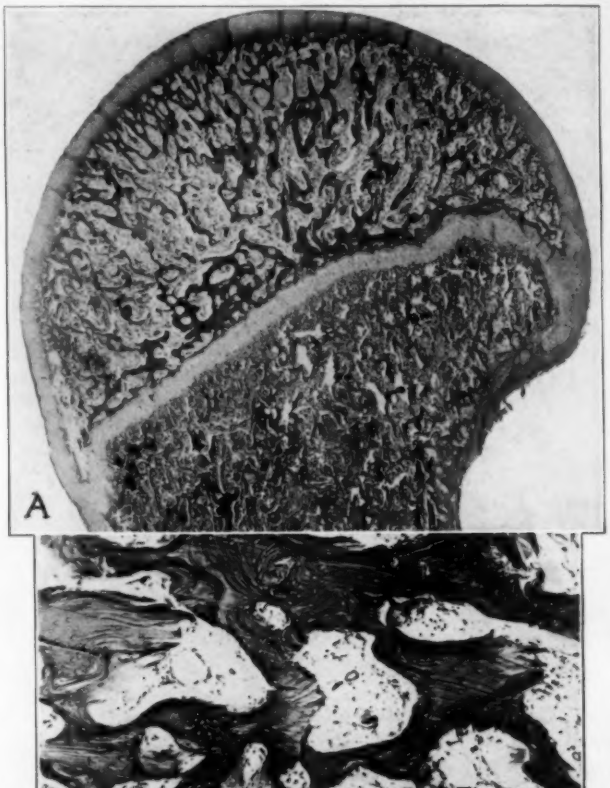

Fig. 3.—*A*, photomicrograph of the femoral head of dog 16, two and one-half months after ligation of the round ligament and stripping of the periosteum from the neck. Almost all of the cancellous bone of the head is necrotic. Reduced from × 12. *B*, photomicrograph of a small area of section shown in *A*. Note the necrosis of the medullary bone and the normal cartilage of the epiphyseal plate. Reduced from × 100.

might lie in some deficiency in the vascular supply of the head of the femur, and consequently this study was undertaken. In a series of

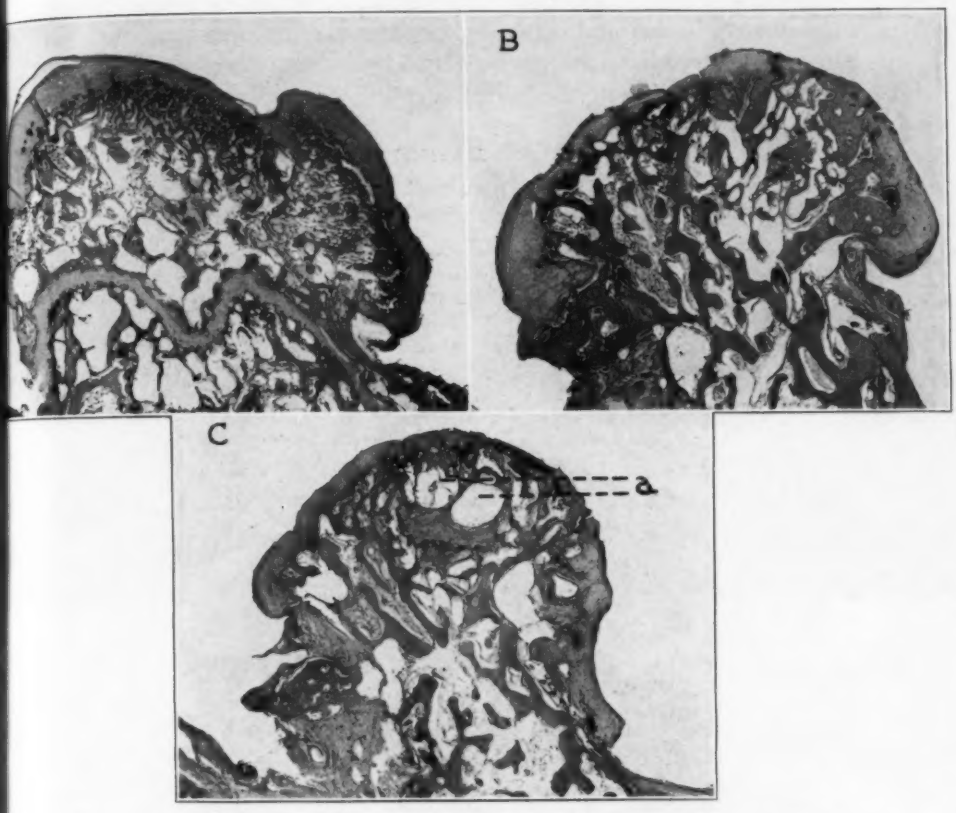

Fig. 4.—*A*, photomicrograph of the femoral head of rabbit 384, three months after ligation of the round ligament and stripping of the periosteum from the neck. The head appears flattened and its surface is irregular as the result of necrosis and atrophy of the underlying cancellous bone. Note the thinning out of the articular cartilage. The large cystlike spaces on either side of the epiphyseal cartilage are artefacts. Reduced from × 20. *B*, photomicrograph of the femoral head of rabbit 367 four months after operation. Note the marked loss of cartilage on the articular surface. The epiphyseal cartilage has disappeared except for a small portion at the left margin, and the bone of the head is in the process of replacement. The cystlike spaces are artefacts. Reduced from × 22. *C*, photomicrograph of the femoral head of rabbit 358 four and one-half months after the same operation as in *A*. Note that the head appears slightly flattened. In certain places the articular cartilage is thin and irregular while in others it is absent. The lateral margins of the articular cartilage overhang the bone of the neck. There are two well defined cysts (*A*) near the articular surface. The other cystlike spaces are artefacts. Reduced from × 18.

experiments on animals, attempts were made to bring about a deficiency of the circulation of the head of the femur, to determine microscopically the changes in the head of the femur after varying periods of time and to see if the resultant changes simulated in any way the clinical syndrome termed Legg-Calvé-Perthes' disease.

METHOD

Five dogs and twelve rabbits were used. The ages of the dogs varied from 2 to 4 months and the ages of the rabbits from 2 to 3 months. Young animals

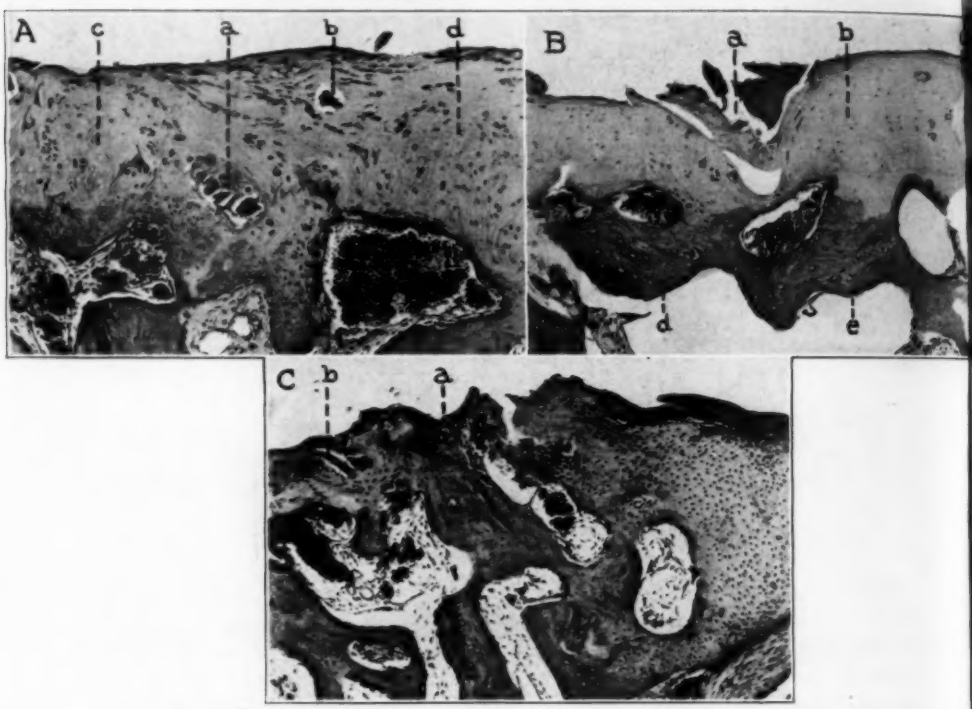

Fig. 5.—*A*, photomicrograph of a portion of the articular cartilage from figure 4 *B*, showing areas of necrosis (*a* and *b*) within the substance of the cartilage and necrotic cartilage cells (*c* and *d*). Reduced from × 120. *B*, photomicrograph of another portion of the articular cartilage shown in figure 4 *B*, revealing a more advanced stage of necrosis. The indentation (*a*) contains a piece of necrotic cartilage. Note the degenerated cartilage cells at *b* and *c* and the degenerated bone cells at *d* and *e*. Reduced from × 135. *C*, photomicrograph of a third portion of the articular cartilage shown in figure 4 *B*, showing a small area in which the articular cartilage has disappeared, with the result that the bone (*a*) is on a level with the cartilage of the surface. The bone cells near the articular surface are necrotic. There is another spicule of dead bone at *b*. Reduced from × 120.

were chosen so that the epiphyses might show active growth of bone and cartilage. Inhalation ether anesthesia was employed in all cases. With aseptic technic the

hip joints were opened through an anterior superior incision. The blood vessels of the femoral head were interrupted according to one of the several methods to be described later, and the incisions were closed with fine silk sutures. Special attention was given to the reapproximation of the subcutaneous tissues and skin, and the wounds were sealed with collodion dressings. Animals in which infection of the hip joint developed were discarded. Roentgenograms were made following the operation and at the time of the autopsy. The animals were killed by electrocution, and autopsies were performed at periods of time varying from two weeks to four and one-half months after the operation. Cultures were taken from the hip joints

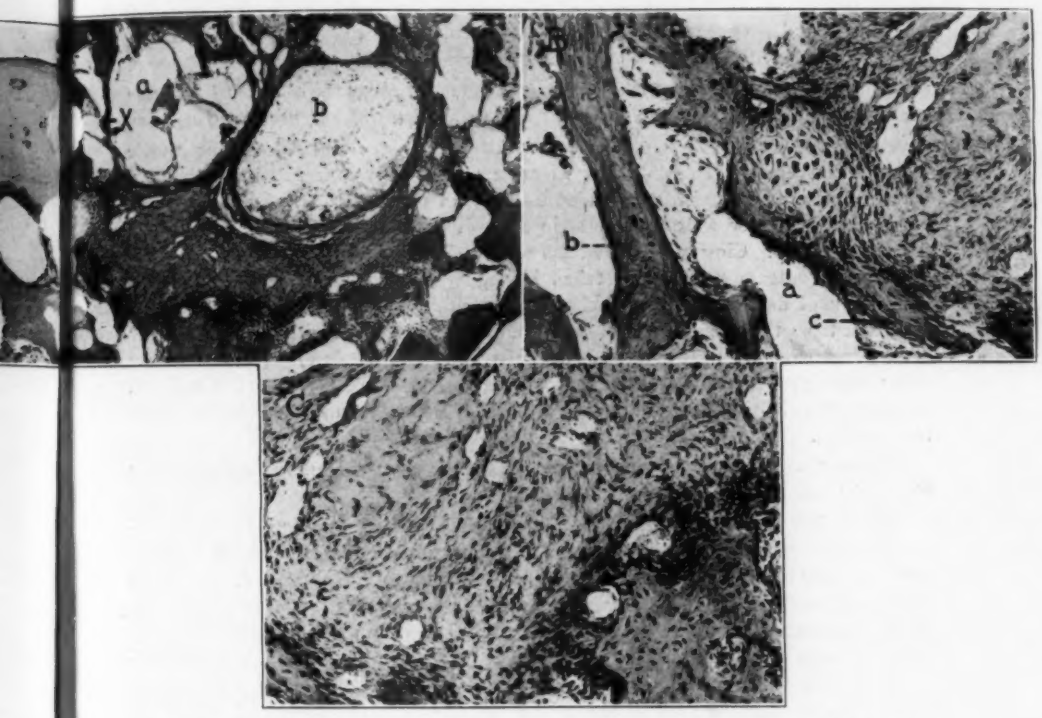

Fig. 6.—*A*, photomicrograph of the two cystic areas shown in figure 4 *C*. Cyst *a* contains a bone trabecula, part of which is necrotic (*X*). This cyst appears to be younger than cyst *b*, which is surrounded by fibrous tissue. Note the metaplasia of fibrous tissue with the formation of cartilage and new bone. *B*, photomicrograph showing a nest of young cartilage cells (*a*) of *A*. Note the spicule of old bone (*b*) to the left, and the spicule of new bone (*c*) next to the cartilage. Reduced from × 155. *C*, photomicrograph of an area from *A*, showing new bone in the lower right corner. Note the vascular fibroblastic tissue which surrounds the new bone. Reduced from × 150.

which were operated on, and the upper ends of both femurs (the normal hip and the one operated on) were removed for gross and microscopic examination.

Three groups of experiments were performed. A description of a typical experiment in each group is given.

GROUP A.—*Alcohol injected into the periosteum of the neck of the femur.*

Dog 4 was 2 months of age. The right hip joint was opened through an anterosuperior incision. The capsule was incised transversely and, through a very fine hypodermic needle, several minims of a solution of 95 per cent alcohol was injected into the periosteum of the neck of the femur and into the overlying synovial membrane. The capsule of the joint was not resutured. The muscles and other soft tissues were closed by sutures of fine silk, and the wound was sealed with collodion. The hip joint was not immobilized. Roentgenograms of both hips were taken shortly after the operation and at the time of the autopsy. The animal was killed two months after the operation, cultures were taken from the hip joint and microscopic sections of both femoral heads were made. Similar experiments were done on dogs 3 and 5 except that in these two animals the condition was allowed to progress further, that is, for three and four months.

GROUP B.—*Alcohol injected into the periosteum of the femoral neck; periosteum also stripped back from the epiphyseal line to the base of the neck of the femur.*

Rabbit 334 was 2 months old. The right hip joint was exposed and the capsule incised transversely. A solution of 95 per cent alcohol was injected into the periosteum and synovia which surrounded the neck of the femur. A fine knife and a small blunt dissector were used to strip the soft tissues from the head back to the base of the neck. Closure of the wound was made by means of interrupted fine silk sutures. Roentgenograms were taken immediately after the operation and again at the time of the autopsy, two weeks later. Cultures were taken from the synovial fluid and from the tissue fluids of the synovial membrane. At this time the upper ends of both femurs were removed for gross and microscopic examination. Three other experiments of the same type were performed on rabbits 218, 358 and 396, the first animal being killed after two and one-half months and the other two after four months.

GROUP C.—*Round ligament ligated with silk suture; periosteum stripped from the neck; silk ligature placed around the neck.*

Rabbit 384 was 2½ months old. The femoral head was exposed as in the previous experiments. By pulling the great trochanter laterally the round ligament was stretched enough to allow the head of the femur to be subluxated. By means of a small curved suture carrier a heavy silk ligature was made to encircle the round ligament and was tied around that structure. Then a circular incision was made through the periosteum at the junction of the head and neck, and the periosteum along with the reflected portion of the synovial membrane was stripped back to the base of the neck of the femur. A silk ligature was placed around the neck to insure the interruption of all of the blood vessels in the periosteum. The wound was closed in the usual manner. Roentgenograms were taken after the operation and again at autopsy, three and one-half months later. At the autopsy, cultures were taken from the hip joint, and the upper ends of both femurs (the normal hip and the one operated on) were removed for gross and microscopic examination. Ten similar experiments were performed on animals 16, 225, 335, 338, 384, 365, 367, 399, 26 and 358. The first four were killed after two and one-half months, the next two after three months, the next two after four months and the last two after four and one-half months.

RESULTS

GROUP A.—In the three dogs comprising this group there were no disturbances in the growth of the head or neck of the femur. Examina-

tion of the gross specimens showed a moderate amount of fibrosis and thickening of the synovial membrane. The anterior portion of the joint capsule was adherent to the periosteum of the neck. The histologic pictures of the femoral heads showed nothing of importance. There was some thickening and fibrosis of the periosteum of the neck at the sites where the injections of alcohol had been made.

GROUP B.—There was no gross evidence of disturbance of growth in any of the cases in this group. In the first case the autopsy was performed two weeks after operation, and the sections showed that vascular fibrous tissue and periosteum had already grown across the surface of the neck which had previously been denuded. In the other three cases microscopic examination of the joint cartilage showed areas in which the cartilage cells were crowded together and had lost their orderly arrangement. The crowding of cells appeared to be due to the loss of matrix. In a few places, the matrix showed swelling and fibrillation. A few cartilage cells stained poorly, showing a marked contrast to the deeply stained cells in their immediate neighborhood. The bone trabeculae showed a few small areas in which the cells were necrotic, but otherwise there was no change. The bone marrow appeared fatty and contained only small numbers of myeloid cells. The epiphyseal cartilage plates were not abnormal. Except for a moderate increase in the fibrous tissue of the periosteum nothing unusual was observed in the microscopic sections of the femoral necks.

GROUP C.—In the nine cases of this group the round ligament was ligated with a silk suture and the periosteum stripped back from the head to the base of the neck. In addition, to insure obstruction of all of the periosteal blood vessels, a silk ligature was tied about the neck. In every case except one, examination of the gross specimens revealed evidence of disturbance of the growth of the head. The round ligaments were smaller than normal and apparently fibrosed. In six of the cases the head appeared flattened and in places the cartilaginous surfaces were roughened and depressed. In the other three cases the cartilaginous surfaces appeared regular in outline, but apparently were thinned in places. In two of the latter cases, there also was gross evidence of early ostearthritic roughening of the bone at the margins of the head of the femur.

The microscopic observations in all cases of group C were similar, and a résumé of these changes in a typical case is given: The cartilage of the head showed an irregular surface and a lack of uniformity in thickness (fig. 4 *A, B* and *C*). The average thickness was about two thirds of the normal. In a few places, the cartilage was absent, leaving the underlying bone exposed (figs. 4 *B* and 5 *C*). There were numerous foci in which the nuclei of the cartilage cells were stained only

faintly with eosin or not stained at all (fig. 5 *A* and *B*). Such unstained nuclei undoubtedly indicated death of cells. The cartilage matrix showed marked variation in its stain, having normal areas of light blue intermingled with areas of red. Fragments of red-stained tissue débris, apparently derived from cartilage matrix, were found on the surface of the cartilage, as well as in its substance (fig. 5 *A* and *B*). Many of the bony trabeculae of the head were irregular in size and smaller than normal. In places these trabeculae were absent, having been replaced by fibrous tissue or cysts (fig. 4 *C*). In many places, especially beneath the cartilaginous surface of the head, the bone cells were either partly or completely degenerated (fig. 5 *B* and *C*). In a few areas, not only were the bone cells necrotic, but the bone matrix had assumed a granular crumbly appearance with roughened edges (fig. 6 *A*). The bone marrow was fibrosed more than normal. In one section (fig. 6 *A*) there were two large cysts, one of which was in an early stage of formation and had an irregular bit of necrotic bone in the center and another bit at the edge. There was a slight degree of fibrosis along the wall. The other cyst was well lined by a thick layer of fibrous tissue which was partly hyalinized and, in part, very cellular. In one portion of the cellular area could be seen transformation of the fibroblast-like cells into typical new bone and, in another portion, into typical hyaline cartilage (fig. 6 *A*, *B* and *C*). The bone marrow of the neck was largely fatty, being in marked contradistinction to that of the normal femur which was more cellular. The cultures which were taken from the hip joints did not show any evidence of bacterial growth.

COMMENT

In the experiments under group A attempts were made to produce osteochondritis by the method of Bentzon, that is, by the injection of alcohol into the periosteum of the neck of the femur. No important changes were observed. The bone and cartilage remained normal, and there was no flattening or fragmentation of the head. The epiphyseal cartilages and the femoral necks were in no way different from those of the control hips of the opposite side.

In the cases of group B, the periosteum and the reflected portion of the synovial membrane was stripped from the chondro-osseous margins of the head to the base of the neck. Alcohol was injected into the periosteum in order to increase the amount of fibrosis and to delay the formation of a new vascular supply. Microscopic sections of those cases showed nothing of importance except for a few very small areas of aseptic necrosis of bone. Apparently the circulatory embarrassment was sufficient to cause only a limited amount of necrosis, which was reparable without gross changes in the head.

In the last group of experiments (group C), the periosteum was stripped from the neck as in the preceding cases, and in addition the round ligament was tied with a silk suture. Since the epiphyseal cartilage plates were intact there followed, necessarily, a severe interruption of the blood supply to the femoral head. In the first experiment of group B, it was seen that new blood vessels had bridged the gap in the periosteum after two weeks. Therefore, in the experiments in group C, it was believed that the circulatory deficiency of the head lasted for only the short period between the time of operative interference and the time when the collateral supply became effective.

The results of the circulatory disturbances were quite constant in all of the cases in the last series. In all of the animals except one, gross examination revealed roughening and slight flattening of the head. In this exception (dog 16, fig. 3 *A* and *B*) gross examination showed nothing particularly abnormal; there was no deformity of the head, and the articular cartilage was smooth and of almost uniform thickness. Microscopic examination, however, showed that practically all of the bone cells of the head were necrotic and that the bone marrow, which consisted largely of fatty tissue, also was necrotic. These changes were interpreted as the early stages of massive aseptic necrosis. We believe that flattening and fragmentation would have followed, provided the condition had been allowed to progress for a longer period of time.

Microscopic examination of the other cases in group C showed uniform pathologic changes. The characteristic changes in the head were patchy, aseptic necrosis of the bone, accompanied by a few areas of necrosis of the articular cartilage. Active repair of bone and cartilage was seen bordering on the areas of necrosis. As the result of weight-bearing on the affected bone, the heads showed gross roughening and flattening of the articular surfaces. Of particular interest were the well defined cystic spaces which were found in the marrow cavities. Apparently these cystic spaces represented areas of degeneration of medullary bone or of the marrow tissues.

CONCLUSIONS

Vascular disturbances of the head of the femur were produced in animals by ligation of the round ligament and by stripping the periosteum from the neck of the femur.

Several months following these procedures the femoral heads showed gross and microscopic changes which were similar to those found in the human disease known as Legg-Calvé-Perthes' disease or osteochondritis of the head of the femur.

PERIARTERIAL SYMPATHECTOMY IN FRACTURES

AN EXPERIMENTAL STUDY

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One of the essential factors in the healing of any fracture is a good and free supply of blood. This was first emphasized by Hilgeneiner,[1] Bier [1] and others, who advised the institution of measures to promote passive hyperemia in an effort to increase the variable phenomena usually present in all fractures. Leriche [2] has shown that following any injury, a reflex vasoconstriction occurs which is soon followed by vasodilatation about the area of the initial trauma. If, however, a periarterial neurectomy or a ganglionectomy is performed, the primary contraction of the involved vessels is followed within a few hours by a vasodilatation of the arterial tree and a marked increase in the blood volume. If these procedures produce an active hyperemia, they should then have a field of usefulness in the treatment of certain groups and types of fractures. Much experimental work has been recorded in recent years dealing with the effect of ganglionectomy and periarterial neurectomy on the healing of fractures.

Palma [3] performed a series of experiments on twelve adult rabbits from 12 to 18 months old. Both radii were fractured, and the lower cervical sympathetic ganglion was removed on one side. The results in the control series and in that in which the fractures were treated by means of ganglionectomy were widely different. Both roentgen and histologic examinations indicated an acceleration of the normal processes of repair on the side subjected to ganglionectomy. Marked connective tissue proliferation was observed five days after the fracture, whereas the control side showed little or none. The transformation of the callus from fibrous tissue into cartilage was almost completed by the tenth day, whereas it scarcely appeared on the control side. Some small

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1. Cited by Uffreduzzi, O.: Arch. ed atti d. Soc. ital. di chir. **31**:1, 1924.
2. Leriche, R.: Ann. Surg. **88**:449 (Sept.) 1928.
3. Palma, R.: Ann. ital. di chir. **4**:85, 1925.

zones of adult bone tissue could be distinguished on the sympathectomized side within fifteen days, while the callus on the control side was merely cartilaginous. Twenty days from the date of fracture, the cartilage on the experimental side had completely changed into bone, whereas on the control side there were small islands of bone instead, and the callus was still mainly cartilaginous. The resorption of callus on the experimental side was well advanced by the thirtieth day, whereas it had hardly started on the control side. The process of ossification on the sympathectomized side was practically completed by the forty-fifth day; that on the control side was one stage less advanced, owing to the presence of bridges and islands of bone in the medullary callus which had not as yet been absorbed. Palma concluded that ganglionectomy accelerated the process of callus formation and transformation about the fracture by inducing a greater blood supply in the entire vascular territory involved.

Uno [4] excised the abdominal sympathetics between the second lumbar and the second sacral vertebra on the right side and fractured both fibulae. Callus formation and healing of fractures were more marked on the ganglionectomized side. Eleven of twelve cases showed definite evidence of the formation of new vessels and a dilatation of the vascular tree with a marked hyperemia. When the fractures of ganglionectomized animals were compared with a series in which periarterial sympathectomy had been performed, the bony union was found to be more marked in the former.

Horton and Craig [5] noted a definite increase in vascularity in the arterial tree of the lower extremity in which the sympathetic innervation had been interrupted by unilateral sympathectomy, ganglionectomy and ramisectomy. This change was not apparent in an experimental animal in which a periarterial sympathectomy neurectomy was performed on the left femoral artery for 5 cm. The stereoscopic x-ray films made six days later on the dead animal were produced by injecting the arterial tree with mercury under its own weight.

Uffreduzzi [6] conducted a series of experiments on young rabbits. He produced bilateral symmetrical fractures of the ulna, and performed a periarterial sympathectomy for about 2 cm. of the axillary and upper portion of the humeral arteries. Roentgen and histologic observations of the processes of repair were made on the sixth, twelfth, twentieth, thirtieth, fortieth and fiftieth days.

It was noted on the twelfth day that the callus on the sympathectomized side was more abundantly vascularized. By the twentieth day,

4. Uno: Arch. f. jap. Chir. **3**:106, 1926.

5. Horton, B. T., and Craig, W. M.: Proc. Staff Meet., Mayo Clin. **4**:240 (Aug. 7) 1929.

6. Uffreduzzi, O.: Arch. ed atti d. Soc. ital. di chir. **31**:1, 1924.

the ossification of the fibrocartilaginous tissue and the callus was noticeably far advanced, and by the thirtieth day, no traces of cartilage were visible. Roentgenograms of the sympathectomized side taken on the fifteenth day showed visible callus which was not apparent on the control side. This callus had increased in size on the twentieth day. Both roentgen and histologic examinations made on the forty-fifth and fiftieth days showed that ossification was taking place. The fusion of the newly formed bone with the fragments took place first on the side that had been sympathectomized, and, in addition, the ossification of the young bone proceeded more rapidly. Sections made on the fortieth and fiftieth days showed that the original callus had been transformed into dense compact bone similar to the old bone from which it could no longer be distinguished and with which it had intimately fused, whereas on the other side it still remained somewhat spongy and vascularized. Uffreduzzi concluded that periarterial sympathectomy seemed to stimulate and accelerate the normal rate of callus development and transformation.

Fontaine[7] performed several experimental studies on dogs. He symmetrically fractured the first metatarsal bones of two animals and performed a periarterial sympathectomy on the right side. He removed different segments of the fractured areas on the twentieth day and found that the fractures of both dogs were united and callus was well developed on the sympathectomized side. However, on the control side, the callus was much less pronounced, and abnormal mobility was still marked. In a third dog, a bilateral transverse fracture of the tibia was produced, and the fragments were held with bronze wire. Sympathectomy was performed on one side. Twenty-three days later, after the piece of wire had been removed, the side subjected to sympathectomy showed advanced union with good callus formation. No union existed on the control side.

Excision of the sympathetic ganglion is undoubtedly a more effective operation and is probably followed by better results than periarterial neurectomy. However, ganglionectomy is more difficult and hazardous, and it is extremely doubtful whether its application in fractures would be justifiable if simpler measures might prove almost as efficacious.

It was our purpose not only to determine the effect of periarterial sympathectomy on the healing of fractures of the leg, but also to ascertain whether evidence of vasodilatation could be demonstrated by injections of the arterial tree with a radiopaque substance. Histologic examinations were not made because this phase has been completely studied and confirmed by other observers and because roentgenologic findings alone are sufficiently satisfactory for the demonstration of the healing of bone and changes in vascularity.

7. Fontaine, R.: Rev. de chir. **64**:95, 1926.

Accordingly, a series of experiments was conducted on twenty dogs, but, owing to accidents of various kinds, only ten animals survived long enough to make the experiment complete.

TECHNIC

The main procedure consisted of simultaneously fracturing with a chisel both tibiae transversely at similar locations and then performing a unilateral femoral periarterial sympathectomy for 5 cm. of the vessel in Scarpa's triangle, the other extremity remaining as a control. Either 3 or 5 cc. of radiopaque iodized rape-seed oil [8] was injected into each femoral artery under direct vision. The entire vascular tree could easily and reliably be visualized by this procedure.

Roentgen studies of the fractures and freshly injected arterial system were made at regular intervals. Studies were made of the radiopaque vessels before

TABLE 1.—*Studies on Changes in Vascularity* *

No. of Dog	Before Sympathectomy (for Control)		Time Interval After Sympathectomy and Fracture	Left Sympathectomy: Both Legs Fractured		Right Leg		Left Leg		Comment. See Protocols
	Right Leg	Left Leg		Right Leg (Control)	Left Leg	Before Fracture	After Fracture	Before Sympathectomy	After Sympathectomy	
10598	0	0	2 wks.	+	++	0	+	0	++	Figures 6 and 7
10609	0	0	10 days	0	++	0	0	0	++	
10622	0	0	2 wks.	0	++	0	0	+	++	
10625	0	0	3 wks.	+	+++	+	+	0	+++	Figures 4 and 5
			6 wks.	—	++++	+	—	0	++++	
10678	0	0	2 wks.	+	++	0	+	0	++	
			35 days	+	+++	0	+	0	+++	
			2 mos.	+	++++	0	+	0	++++	
10685	0	0	2 wks.	+	+	+	++	+	++	Figures 1, 2 and 3
			2 mos.	n.c.	+++	n.c.	++	+	+++	
			2½ mos.	+	++++	+	—	+	++++	
10764	0	0	2 wks.	+	+++	+	+	0	+++	
10789	0	0	2 wks.	0	+++	0	0	0	++	

* 0 indicates no change; +, an increase; —, diminished, and n.c., not comparable.

sympathectomy and before fracture. Similar studies were repeated after fracture and sympathectomy, and again at from seven to ten day intervals, and for varying periods up to ten weeks for vascular studies, and six months for the healing of bone.

The radiopaque substance used for injection was a heavy liquid consisting of 4 parts iodized rape-seed oil, with a specific gravity of 1.289, and 1 part of ethyl olive oil, making a specific gravity of 1.061.

It took considerable time and effort to so standardize the method of injection that satisfactory roentgenograms of the injected arterial tree could be regularly obtained. Attempts were made always to inject a uniform amount of iodized rape-seed oil at the same rate of speed in each experiment. When half of the oil had been injected, roentgen exposures were made while the remainder of the substance was being

8. Frazier, C.: Ann. Surg. **89**:801 (June) 1926.

injected. One great technical difficulty was caused by the fact that a needle of considerable bore had to be employed because of the viscosity of the iodized rape-seed oil. When injections had to be repeated on the same sympathectomized artery, the large needle would occasionally damage the wall of the neurectomized vessel, resulting in fatal hemorrhage.

A study of tables 1 and 2 and the protocols will reveal that the experimental procedure varied in details, especially as far as the time of the arterial injections were concerned. This was done to make every effort carefully to control the experiment. While the protocols are given in detail, the results of these experiments can best be appreciated by a study of tables 1 and 2, respectively.

TABLE 2.—*Studies on Callus and Bony Union*

	Callus			Bony Union			
No. of Dog	Time Interval	Right Leg (Control)	Left Leg (Sympathectomy)	Time Interval	Right Leg (Control)	Left Leg (Sympathectomy)	Comment: See Protocols
10609	1 mo.	None	++	(Death)			
10622	3 wks.	+	++	1 mo.	None	Union	
10625	1 wk.	+	+	1 wk.	None	Partly	Figures 4 and 5
	2 wks.	++	+	2 wks.	None	Complete	
	6 wks.	+++	+	6 wks.	Fibrous	Complete	
10678	20 days	++	++	20 days	None	None	
	35 days	++	+++	35 days	None	Partial	
	50 days	++	+++	50 days	None	Complete	
10685	20 days	+++	+	20 days	None	Union	Figures 1, 2 and 3
	40 days	+++	++	40 days	None	Union	
10765	2 wks.	+++	+	2 wks.	Fibrous	Complete	
10789	3 wks.	+	+++	(Death)			
10892	1 mo.	+	+++	1 mo.	None	Partial	Figures 8 and 9
	2 mos.	++	+++	2 mos.	None	Complete	
10893	3 wks.	None	+	3 wks.	None	None	
	5 wks.	++	++	5 wks.	Partial	Partial	
	6 mos.	++	++	6 mos.	Partial	Complete	

PROTOCOL 1 (dog 10598).—*Experimentation.*—Oct. 24, 1930: The right femoral artery was exposed in Scarpa's triangle and 5 cc. of iodized rape-seed oil was injected into it; roentgenograms of the lower extremity were then taken.

The left femoral artery was similarly exposed; 5 cc. of iodized rape-seed oil was injected, and roentgenograms of the extremity were taken.

October 28: The left femoral artery was again exposed in Scarpa's triangle and sympathectomized for 5 cm. of its extent; 5 cc. of iodized rape-seed oil was then injected. Roentgenograms were then taken.

The right femoral artery was then similarly exposed; 5 cc. of iodized rape-seed oil was injected, and roentgenograms were taken.

November 14: The right and left femoral arteries were again exposed, 5 cc. of iodized rape-seed oil being injected into each. Roentgenograms of each extremity were then taken.

November 28: The right femoral artery was exposed in Scarpa's triangle, and a sympathectomy was then done for a distance of 5 cm. Roentgenograms were then taken.

December 4: The animal died of secondary infection of a hematoma about the sites of the wounds. The tibial vessels of both sides were dissected out, and no gross difference was detected.

Studies of Roentgenograms.—Oct. 24, 1930: The injection of the left femoral artery was unsuccessful, but that of the right femoral artery was satisfactory.

October 28: The left vascular bed was greater than that of the right side and was increased over that of October 24.

The right vascular bed was increased over that of October 24.

November 14: The left vascular bed, the sympathectomized side, was definitely increased over that of the right side, and over that of October 28.

The right vascular bed remained unchanged from that of October 28.

November 28: After sympathectomy, the right vascular bed showed no change over the previous observation.

Fig. 1 (dog 10685).—Both legs were fractured. Sympathectomy was performed on the left side. Both femoral arteries were injected with iodized rape-seed oil. Many more small arteries are visible on the left than on the right.

Comment.—On referring to figures 6 and 7, it is seen that the richness of the vascular bed and the increase in the number and the caliber of the arteries are quite evident on the side of the sympathectomy (left leg).

PROTOCOL 2 (dog 10609).—*Experimentation.*—Oct. 31, 1930: The left femoral artery was exposed in Scarpa's triangle and 5 cc. of iodized rape-seed oil was injected; then roentgenograms of the lower extremity were taken. A periarterial sympathectomy was then done on the left femoral artery; 5 cc. of iodized rape-seed oil was injected, and roentgenograms were taken. A lateral ligature was necessary to control the bleeding from the artery at the site of the needle puncture.

The right femoral artery was exposed in Scarpa's triangle, 5 cc. of iodized rape-seed oil was injected, and roentgenograms of the right lower extremity were taken.

Each tibia was then fractured by a chisel, through incised wounds at similar levels.

November 10: The left femoral artery was again exposed in Scarpa's triangle, and 5 cc. of iodized rape-seed oil was injected, and roentgenograms were taken.

The right femoral artery was again exposed, and 5 cc. of iodized rape-seed oil was injected, and roentgenograms were taken.

The left femoral artery was irretrievably damaged, causing an immediate fatal hemorrhage. After death, 3 cc. of iodized rape-seed oil was injected into each femoral artery, and roentgenograms were taken.

Fig. 2 (dog 10685).—Roentgenograms taken twenty days after those in figure 1. The union is almost perfect on the left side. The right leg (control) shows callus, but the line of fracture is not obliterated.

Study of Roentgenograms.—Oct. 31, 1930: The vascular bed on the left side before sympathectomy was slightly less than on the right side, but after the sympathectomy it was definitely greater. The left femoral artery, while not dilated, was larger in caliber than the right.

The fractures were found to be comparable.

November 10: There was a distinct increase in vascularity on the left side over the previous observation on October 31. The right side showed no change when compared with the observation of October 31.

On the left side there were no union and some displacement of the fragment. There was evidence of beginning callus formation along the ends of the fragments.

There were no displacement of fragments and no callus formation on the right side.

Comment.—The findings on the left side, when compared with those on the right side, seem to prove that the vascularity on the sympathectomized side was definitely increased.

The sympathectomized side alone showed callus formation. Bony union was not determined, as the animal died too soon.

PROTOCOL 3 (dog 10622).—*Experimentation.*—Nov. 18, 1930: The right tibia was fractured through a small incised wound at the junction of the upper and middle

Fig. 3 (dog 10685).—Roentgenograms taken about two and one-half months after those in figure 2. There is complete healing on the left side. The right leg shows considerable callus. The fracture line is still unobliterated.

thirds. The right femoral artery was exposed in Scarpa's triangle, 3 cc. of iodized rape-seed oil was injected, and roentgenograms of the right lower extremity were taken.

The left tibia was fractured at approximately the same site as the right. The left femoral artery was exposed in Scarpa's triangle, 3 cc. of iodized rape-seed oil was injected, and roentgenograms were taken. A sympathectomy was then performed on the left femoral artery. The vessel immediately contracted.

November 28: Roentgenograms of both lower extremities were taken.

December 5: The wounds of both sides were healed.

The right femoral artery was again exposed in Scarpa's triangle, and was found to be embedded in organized fibrous tissue. Three cubic centimeters of iodized rape-seed oil was injected, and roentgenograms were taken.

The left femoral artery was then exposed and was found to be similarly embedded in organized adhesions. Three cubic centimeters of iodized rape-seed oil was injected, and roentgenograms were taken. A large hemorrhage resulted from the site of the injection, necessitating ligation of the artery and vein before it could be controlled.

December 12: Roentgenograms of both lower extremities were taken. The general condition of the animal was good, though the animal was unable to bear weight.

December 22: Roentgenograms of both lower extremities were taken.

April 20, 1931: The dog died.

Study of Roentgenograms.—Nov. 18, 1930: The left (sympathectomized) side showed a greater vascular bed than the right. The fractures were practically similar.

November 28: No injection was made.

The fracture remained similar. There was moderate callus on the left side, but none on the right side.

December 5: The left vascular bed showed an increase in general over the original observation of November 18.

The right side showed an increase in vascularity about the site of fracture, but not elsewhere. The left side, compared with the right, showed a marked increase in vascularity, especially about the fracture site.

The left side showed no increase in callus. The right showed beginning callus formation, which was definitely less than that on the left side.

December 12: There was marked callus on both sides, with a greater amount on the left side. The left side showed complete union, while the fragments of the right side were not united.

December 22: The left side showed a further increase in callus, with complete union. There was no change in the callus on the right side and no further union.

Comment.—This experiment again illustrates the decided increase in the vascularity of the left leg.

Within a three week interval, there was slight callus on the right side, but more callus on the left; furthermore, within a month's interval no bony union had taken place on the control side (right), and on the left side a firm bony union had already been established.

Protocol 4 (dog 10625).—*Experimentation.*—Nov. 21, 1930: The right and left tibiae were fractured by a chisel through small incised wounds at similar levels. The right femoral artery was exposed in Scarpa's triangle, 3 cc. of iodized rape-seed oil was injected, and roentgenograms of the lower extremity were taken. A sympathectomy was performed on the left femoral artery for 5 cm. of its extent, after the left femoral artery had been exposed, given an injection and x-ray similar to the right.

November 28 and December 5: Roentgenograms of both extremities were taken.

December 19: The left femoral artery was again exposed in Scarpa's triangle, 3 cc. of iodized rape-seed oil was injected, and roentgenograms were taken. The right femoral artery was similarly exposed, 3 cc. of iodized rape-seed oil was injected, and roentgenograms were taken.

Jan. 6, 1931: Both femoral arteries were again exposed, 3 cc. of iodized rape-seed oil was injected into each vessel, and roentgenograms were taken.

March 10: Both femoral arteries were exposed and separately given injections of 3 cc. of iodized rape-seed oil, and roentgenograms were taken.

Studies of Roentgenograms.—Nov. 21, 1930: The right vascular bed was slightly greater than the left before sympathectomy. The fractures were not complete, but were similar and comparable.

November 21 and December 5: The fracture line on the left was almost obliterated.

On the right there was a small amount of callus.

December 12: The vascular bed after sympathectomy was greater on the left side than on November 21, and was more marked than on the right side.

On the right side, there was no change over the observation of November 21.

There was complete union on the left side. On the right side there was more callus, but partial union.

December 19: There was no change over the observation of December 12.

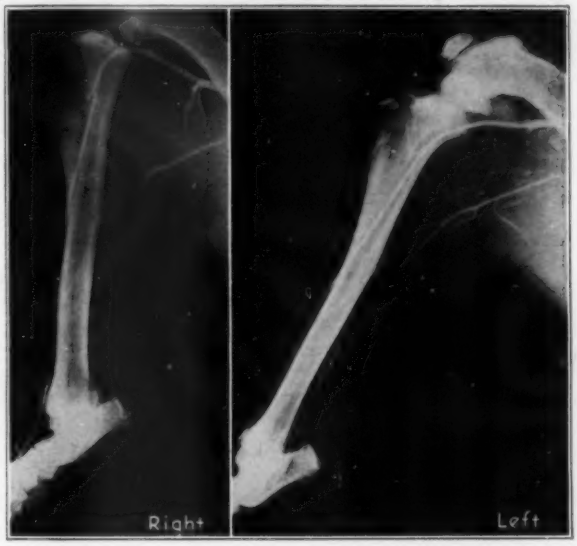

Fig. 4 (dog 10625).—Both tibiae were fractured. Sympathectomy was performed on the left. Note the richness in vascularity on the left side. The fracture line of the left tibia is not clearly shown here owing to underexposure.

Jan. 6, 1931: The left side showed a marked increase in vascularity which was greater than that on the right side. The right side showed a diminution in vascularity when compared with that of December 12. The left showed complete union. The right showed more callus but no union.

March 10: The injections were unsatisfactory and inconclusive. Both fractures were well healed, but resorption was more complete on the left.

Comment.—Three weeks after the left leg was sympathectomized, there was a decided increase in vascularity on that side. Note the complete bony union on the left in figures 4 and 5.

Findings during one-half and six week intervals showed more callus produced on the right. However, there was complete bony union on the sympathectomized side and only fibrous union on the control side.

PROTOCOL 5 (dog 10678).—*Experimentation.*—Jan. 13, 1931: The right and left tibiae were fractured by a chisel through small incised wounds at similar levels. The right femoral artery was exposed in Scarpa's triangle, 3 cc. of iodized rape-seed oil was injected, and roentgenograms of the extremity were taken.

The left femoral artery was similarly exposed, 3 cc. of iodized rape-seed oil was injected, and roentgenograms were taken. Sympathectomy was then performed on the left femoral artery for 5 cm. of its extent.

January 27: Both femoral arteries were again exposed in Scarpa's triangle, 3 cc. of iodized rape-seed oil being injected into each. Roentgenograms were taken. There was a considerable amount of reaction about the sites of fracture, with a seropurulent discharge.

February 3: Roentgenograms of both lower extremities were taken.

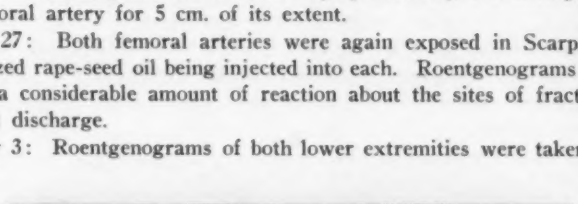

Fig. 5 (dog 10625).—Roentgenograms taken six weeks after those in figure 4. There is a marked increase in vascularity on the side of sympathectomy. Union is more complete on the left. (Unfortunately the injected main right arteries are not included in the print. The original films show them to be equally injected and comparable.)

February 17: Both femoral arteries were exposed, 3 cc. of iodized rape-seed oil was injected, and roentgenograms of the lower extremities were taken.

March 3: Both femoral arteries were again exposed in Scarpa's triangle, 3 cc. of iodized rape-seed oil was injected, and roentgenograms were taken. The dog was chloroformed on this date.

Study of Roentgenograms.—Jan. 13, 1931: The vascular beds of both sides were practically the same. The fractures were similar and comparable.

January 27: On the left (sympathectomized) side the vascular bed was decidedly increased over that on the right, and also over the original vascularity on the left side on January 13. The increase was especially about the fragments.

On the right side the vascular bed was increased over the observation of January 13, especially about the fragments.

February 3: Both sides showed an equal amount of callus; there was no evidence of union.

February 17: The vascular bed on the left showed a general increase over that of January 27, and was decidedly greater than that on the right side. Some of the vascularities showed an increase in caliber.

The vascular bed on the right showed an increase only about the site of fracture.

Both sides showed a definite increase in callus. The density and amount were greater on the left side, which also showed partial union.

March 3: The vascular beds remained unchanged over January 27, with the left side being greater than the right.

The left side showed an increase in callus and complete union. The right side showed a slight increase in callus and no union.

Comment.—Observations noted in three consecutive periods (table 1) seemed to show that there was a marked increase in the vascular beds on the sympathectomized side. It also was observed that the increase in vascularity was more pronounced in later experiments.

There was a considerable amount of callus about the fragment of the tibia in both legs, but it was more pronounced on the left, where the sympathectomy was performed. Observation was continued at twenty, thirty-five and fifty day intervals. At no time was there any evidence of union on the right side. Union commenced on the thirty-fifth day on the left side, and became complete in less than two months.

Protocol 6 (dog 10685).—*Experimentation.*—Jan. 20, 1931: The right and the left tibiae were fractured by a chisel through small incised wounds at similar levels. The right femoral artery was exposed in Scarpa's triangle, 3 cc. of iodized rape-seed oil was injected, and roentgenograms were taken. The left femoral artery was similarly exposed, 3 cc. of iodized rape-seed oil was injected, and roentgenograms were taken. A sympathectomy was then done on the left femoral artery for 5 cm. of its extent.

January 27: Roentgenograms of both lower extremities were taken.

February 3 and 10: Both femoral arteries were exposed, 3 cc. of iodized rape-seed oil was injected, and roentgenograms were taken.

February 24, March 31 and April 7: Both femoral arteries were exposed in Scarpa's triangle. Three cubic centimeters of iodized rape-seed oil was then injected into each, and roentgenograms of the extremities were taken.

Studies of Roentgenograms.—Jan. 20, 1931: There was no difference in the vascular beds of either side. The fractures were similar and comparable.

January 27: There was slight callus on the left side. On the right side there was no callus, and there was a slight separation of the fragments.

February 3: The vascular beds about the fragments were equally increased on both sides. There was no change on the left side with partial union. On the right side there was slight callus, without union.

February 10: There was complete union on the left, with an increase in callus. On the right there was no union. The callus was increased and was greater than that on the left.

February 24: On the left the injection was unsuccessful. On the right there was a definite increase in vascularity over February 3.

There was complete union with an increase in callus on the left. On the right there was no union. The callus was increased.

March 31: There was a definite increase in vascularity over the observation of the right and left sides on February 24.

On the right side, injection was unsuccessful, and the experiment was therefore not comparable.

The fracture line on the left side was obliterated. On the right, callus was increased, but there was no union.

April 7: The vascularity on the left side was greater about the fragments when compared with that side on March 31, and was greater than that on the right side.

The vascularity on the right side was diminished when compared with that on the right side on February 3.

Callus was slightly increased on the left, but was less than on the right. There was complete union, with obliteration of the fracture line.

The right side was unchanged. There was no union.

Comment.—At consecutive observations of two weeks, two months and two and a half months, the roentgen findings definitely showed an increase in vascularity

Fig. 6 (dog 10598).—Sympathectomy was performed on the left side. Note the relative richness in vascularity on the left side.

and dilatation of the capillary bed on the sympathectomized side. It is interesting to note that the vascular bed on the control side diminished considerably by the time of the last observation (figs. 1, 2 and 3). In addition, there was complete bony union on the side that had been sympathectomized, and there was no union on the control side.

Protocol 7 (dog 10764).—*Experimentation.*—March 3, 1931: The right and left tibiae were fractured by a chisel through small incised wounds at similar levels.

The right femoral artery was exposed in Scarpa's triangle, 3 cc. of iodized rape-seed oil was injected, and roentgenograms of the lower extremity were taken.

The left femoral artery was similarly exposed, 3 cc. of iodized rape-seed oil was injected, and roentgenograms were taken.

A sympathectomy was then done on the left femoral artery for a distance of 5 cm.

March 10: Roentgenograms of both lower extremities were taken.

March 17: The left femoral artery was again exposed in Scarpa's triangle. While injecting the iodized rape-seed oil, the vessel ruptured, necessitating ligation to control the hemorrhage. Three cubic centimeters of iodized rape-seed oil was injected after this, and roentgenograms were taken.

The right femoral artery was exposed and ligated, and then 3 cc. of iodized rape-seed oil was injected. Roentgenograms were taken. The animal was then chloroformed. Specimens of the fracture sites were removed. The right side showed fibrous union, and the left side showed solid union. The femoral and tibial arteries were examined. The vessels of the left side were more dilated than those of the right side.

Studies of Roentgenograms.—March 3, 1931: The left vascular bed (sympathectomized side) was greater than the right. Both fractures were incomplete but comparable.

Fig. 7 (dog 10598).—Roentgenograms taken two weeks after those in figure 6. There is a further increase in vascularity on the left side.

March 10: There was no evidence of callus, and there was no change in the fractures.

March 17: The vascular bed on the left was definitely increased over the original observation.

The injection was unsuccessful on the right side.

There was evidence of callus on the right but none on the left.

Comment.—Two weeks after the control pictures were taken, the sympathectomized side presented a marked increase in vascularity. On the right side, however, there was very little increase in the vascular bed. These findings again emphasize that there appears to be a definite relation between vascularity and sympathectomy.

No deductions can be drawn on the question of callus and bony union, because the animal had to be chloroformed after two weeks of observation.

PROTOCOL 8 (dog 10789).—*Experimentation.*—March 10, 1931: The right and left tibiae were fractured by a chisel through small incised wounds at similar levels. The left femoral artery was exposed in Scarpa's triangle, and a sympathectomy was done for a distance of 5 cm.

March 24: The left femoral artery was again exposed in Scarpa's triangle, and 3 cc. of iodized rape-seed oil was then injected. Roentgenograms of the lower extremity were then taken.

The right femoral artery was similarly exposed, 3 cc. of iodized rape-seed oil was injected, and roentgenograms were taken.

April 7: Each femoral artery was exposed, 3 cc. of iodized rape-seed oil was injected, and roentgenograms of the lower extremities were taken.

June 24: The animal died while being used for other experimental work.

Fig. 8 (dog 10892).—Both legs were fractured. The left side was sympathectomized. Compare with figure 9.

Studies of Roentgenograms.—March 10, 1931: Both fractures were similar and comparable.

March 24: The vascular bed was greater on the left (sympathectomized) side than on the right.

No callus was present on either side.

April 7: The vascularity on the left was increased in amount, especially about the fragments, and was greater than that on the right.

The vascularity on the right was increased over that of March 24.

There was no increase in callus and bony union on the left side over March 3, but the callus was greater in amount than that on the right side. There was no union.

On the right, there was an increase in callus over the observation of March 24, but there was no union.

Comment.—After repeated studies, the nonsympathectomized side (the right leg) failed to show any change in the vascular picture, while the left side seemed to appear rich in the vascular bed.

There was considerable callus on the sympathectomized side (left). The study of the bony union could not be accomplished, owing to the death of the animal.

Protocol 9 (dog 10892).—*Experimentation.*—April 14, 1931: The left femoral artery was exposed in Scarpa's triangle, and a periarterial sympathectomy was done for a distance of 5 cm.

Fig. 9 (dog 10892).—Roentgenograms taken two months after those in figure 8. Both sides show marked callus, particularly on the left side. There is no bony union on the control (right) side. The left side shows union.

Both tibiae were fractured by a chisel through small incised wounds at similar levels. Roentgenograms of both lower extremities were then taken.

No injections of iodized rape-seed oil were made in this experiment.

April 21 and 28, May 8, 15 and 22 and June 2 and 12: Roentgenograms of both lower extremities were taken.

August 14: The animal died after being used for other experimental work.

Study of Roentgenograms.—April 14, 1931: The fractures of both tibiae were complete and comparable.

April 21: The left (sympathectomized) side showed slight callus about the fracture; there was none on the right.

April 28: There was marked callus with partial union on the left. On the right, there was slight callus, but no union.

May 8: On the left, there was marked callus with partial union. On the right, there was little callus, but no union.

May 22: The roentgenogram of the left leg was unsatisfactory as the animal moved. On the right, there was a large amount of callus, but no union.

June 2: There was no change over the previous observation.

June 12: There was marked callus on the left, greater than on the right, with almost complete obliteration of the fracture line. On the right, there was marked callus, but no union.

Comments.—Observations were carried on at intervals of one and two months, during which time there was more callus on the left side than on the right. No union had taken place on the right side, but complete union had resulted on the left side (figs. 8 and 9).

Protocol 10 (dog 10893).—*Experimentation.*—April 14, 1931: The left femoral artery was exposed in Scarpa's triangle, and a sympathectomy was done for a distance of 5 cm. Both tibiae were then fractured by a chisel at similar levels, through small incised wounds. Roentgenograms were then taken. No injections of iodized rape-seed oil were made in this experiment.

April 21 and 28, May 8, 15 and 22, June 2 and 12 and October 7 and 22: Roentgenograms of both lower extremities were taken.

Studies of Roentgenograms.—April 14, 1931: The fractures were complete and comparable.

April 21: There was no evidence of healing.

April 28: The fragments of both fractures showed overriding and separation, being more marked on the left side than on the right.

May 8: The left side showed slight callus and more overriding.

May 15: There was no change over the previous observation.

May 22: Both sides showed a large and equal amount of callus. There was partial union on both sides.

June 2: There was no change over the previous observation.

June 12: There was a slight increase in callus on both sides.

October 7: On the left, the fracture was completely healed, and the fracture line was obliterated. On the right, there was a slight deformity. The fracture line was still visible, and there was apparent union.

October 22: There was perfect healing with complete obliteration of the fracture line on the left side.

On the right side, there was complete healing, but the fracture line was still clearly visible.

Comment.—This dog was studied at intervals of three weeks, five weeks and six months. Both sides showed almost equal amounts of callus. There was no bony union at the end of the three week interval, but at the end of six months there was partial union on the control side and firm union on the left side, on which the sympathectomy had been performed.

SUMMARY

Radiopaque visualization of the arterial tree of the lower extremity on which a femoral arterial sympathectomy was performed at Scarpa's

triangle revealed an increasing vascularity in all experiments. This persisted throughout the longest period of observation, that is, ten weeks.

Callus was first detected on the sympathectomized extremities in five dogs, three times on the control extremities, and in one instance, it was doubtful. Firm bony union, however, was evidenced sooner on the sympathectomized side in all animals surviving a sufficient period of observation. Complete bony union, as determined by obliteration of the fracture line, occurred only on the sympathectomized extremity and was never noted on the control side during the period of observation.

COMMENT

The experimental work of others and this study seem to prove that periarterial sympathectomy has a physiologic basis for clinical application in the problem of the repair of fractures. In a series of clinical cases previously reported,[9] femoral periarterial sympathectomy in Scarpa's triangle was performed on seven patients with recent fractures of both bones of the leg. There was a diminution in time of eleven days in obtaining clinical union, and of nineteen days in hospitalization. No case showed a tendency toward delayed union when compared with a control series. In a group of ten cases of delayed union in fractures of the lower extremity which were ununited after an average of seventy days, clinical union resulted twenty-one days after sympathectomy in eight cases.

CONCLUSIONS

1. These experiments of femoral arterial injection seem to show quite definitely that an increased vascularity results from periarterial sympathectomy and that this procedure accelerates bony union.

2. The experimental and clinical evidence seems to justify a further trial of this operation in recent fractures, in those regions in which delay in union is characteristic and in those fractures in which union appears to be delayed.

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9. Colp, R., and Mage, S.: Experiences with Periarterial Sympathectomy in Fractures of the Lower Extremity, J. A. M. A. **97**:1069 (Oct. 10) 1931.

TREATMENT OF PULSATING EXOPHTHALMOS

WITH REPORT OF TWO CASES

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Pulsating exophthalmos, or retrobulbar arteriovenous aneurysm, a lesion first reported by Benjamin Travers in 1809, is a relatively rare condition meriting report whenever seen. An average of about five cases is reported each year. Harkness [1] collected six hundred and twenty-one cases from the literature in his paper published in May, 1930. An exhaustive review of the literature is not attempted here, that angle of the problem having been dealt with ably by de Schweinitz and Holloway,[2] later by Locke [3] and still later by Harkness.

Diagnosis of the lesion usually may be made from the patient's history and appearance alone. The history is fairly typical: After trauma resulting in a period of unconsciousness, the patient has failure of vision or blindness in one eye, unilateral exophthalmos and a rushing, roaring sound in the head synchronous with the pulse. Palpation of the eye commonly discloses a thrill, and auscultation, a bruit synchronous with the pulse.

Autopsy in these cases usually reveals an opening in the internal carotid artery in its course through the cavernous sinus. The lesion tends to be progressive rather than tending to a spontaneous cure, although some cases apparently have cleared spontaneously (Noland and Taylor [4]).

The time-honored treatment of pulsating exophthalmos has been ligation of the artery involved, either abruptly or gradually. Sudden ligation of the internal carotid artery is attended with a high percentage of hemiplegia and other evidences of unilateral cerebral damage. This has led to ingenious devices for closing the artery gradually. An

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From the Cleveland Clinic.

1. Harkness, G. F.: Intracranial Arterio-Venous Aneurysm, Pulsating Exophthalmos, Internat. J. Med. & Surg. **43**:243, 1930.

2. de Schweinitz, G. E., and Holloway, T. B.: Pulsating Exophthalmos: Etiology, Symptomatology, Pathogenesis and Treatment, in Diseases of the Eye; A Handbook of Ophthalmic Practice, ed. 10, Philadelphia, W. B. Saunders Company, 1924.

3. Locke, C. E., Jr.: Intracranial Arterio-Venous Aneurysm or Pulsating Exophthalmos, Ann. Surg. **80**:1 and 272, 1924.

4. Noland, L., and Taylor, A. S.: Pulsating Exophthalmos: Result of Injury, Tr. South. S. A. **43**:171, 1931.

excellent account of these methods is given by Hanford and Wheeler.[5] Other operators have ligated the common carotid artery, retrograde flow from the external to the internal carotid usually being sufficient to prevent cerebral complications. The résumé by Hanford and Wheeler reports 67 per cent of patients cured and 83 per cent cured or improved by primary ligation of the internal carotid artery. After ligation of the common carotid, 46 per cent of patients were cured, and 64 per cent were cured or improved. Locke's statistics were about the same in 1924.

In considering a rational treatment for intracranial arteriovenous aneurysm, one should take into account the principles of treatment of arteriovenous aneurysm elsewhere, as in a leg or an arm.

PRINCIPLES OF TREATMENT

Principle I.—The Hunterian principle of ligation of the involved artery proximal to the fistula (fig. 1 *b*) has long been recognized as inadequate, since collateral circulation promptly bridges over the ligature. Applied to pulsating exophthalmos, this involves ligating the ipsilateral internal or common carotid artery. Ligating the common carotid artery allows a greater degree of anastomosis to continue the lesion, although the immediate morbidity from cerebral accident is lessened.

Principle II.—Ligation of the artery both proximal and distal to the aneurysm (fig. 1 *b* and *c*) may be beneficial when there are very few collateral channels. In these intracranial lesions, the ligatures would be applied to the internal carotid artery in the neck and within the cranium between the circle of Willis and the cavernous sinus (fig. 2 *a* and *c*). The intracavernous portion of the internal carotid artery gives off the ophthalmic artery and a few minute twigs, one anastomosing with the middle meningeal artery and the remainder supplying the pituitary gland. It is by way of these anastomoses that this principle of treatment may be defeated in this lesion.

Principle III.—Ligation of all the arteries and veins involved in the lesion (fig. 1 *b, c, d, e, f* and *g*) has proved, in general, to be the principle of greatest efficacy in treating arteriovenous aneurysm. In the case of pulsating exophthalmos, this would involve ligating the internal carotid artery above and below the cavernous sinus, ligating the ophthalmic artery and isolating by ligature the ipsilateral cavernous sinus. Ligation of the internal jugular vein with the internal carotid artery has been advocated by many writers. This is incomplete as the two cavernous sinuses, unfortunately, communicate through the anterior and posterior intercavernous sinuses, ligation of which would be extremely difficult, if not technically impossible, at present. It seems, then, that the principle most efficacious in controlling other arteriovenous fistulas would fail to be applicable in this instance.

5. Hanford, J. M., and Wheeler, J. M.: Pulsating Exophthalmos, Ann. Surg. **92**:8, 1930.

Principle IV.—Direct closure of the fistula (fig. 1 *a*), while theoretically the method of choice, is rarely feasible in arteriovenous fistulas. In retrobulbar arteriovenous aneurysms actual ligature obviously is impossible within the cavernous sinus. A method of occlusion has been devised by Brooks [6] of Nashville, and has been used by other operators with apparent success, although at present its status is not definitely fixed.

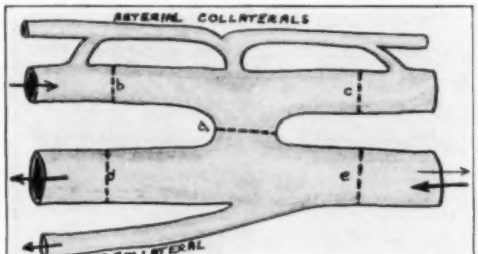

Fig. 1.—Diagrammatic representation of ligations used to control arteriovenous aneurysm.

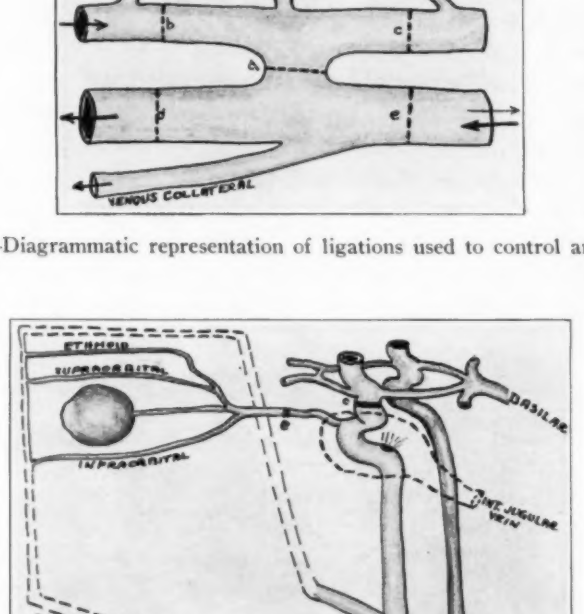

Fig. 2.—Diagram of circulation involved in retro-orbital pulsating exophthalmos and collaterals.

Brooks opened the internal carotid artery in the neck, between clamps, and packed long thin strips of muscle into the artery. The incision in the artery was then closed, and the clamps removed; the blood stream forced the muscle into the fistula, effectually plugging it. The eye in the case described was later lost from thrombosis. In adopting

6. Brooks, C. M., in discussion of Noland and Taylor.[4]

Brooks' technic, we used a smaller muscle embolus, hoping to have the function of the artery, but ligation was necessary later.

This seems a rather radical procedure—sending a muscle embolus toward the brain with all the force of the heart behind it. The embolus is propelled by a force equal to the systolic blood pressure (fig. 3). At the fistula, however, it is acted on by two other forces; at the point of division it may go into the cerebral circulation, against a pressure equal to diastolic blood pressure or 80 mm. of mercury, or it may go into the fistula, where the pressure is very much lower. The embolus takes the course of least resistance and enters the fistula. If it is not large enough to engage the margins of the fistula, it is held by the lacework of fibers in the sinus and can go no further. The combined effect of the embolus and resulting thrombosis closes the opening.

Mechanical devices which accomplish compression of the arteries in the neck by various ingenious pressure bands and springs have maintained many patients in a fair state of health, as in one case reported by Harkness. Another expedient is ligation of the common carotid artery, allowing retrograde blood flow to prevent sudden anemia of the brain, and later ligation of all the branches of the external carotid artery

Fig. 3.—Mechanics of blood flow at point of arteriovenous fistula.

except the internal maxillary and temporal, thus further diminishing the blood flow by reducing the number of anastomoses. This was advocated by Dorrance.[7]

Of course, many patients are considered cured if they are able to continue with their daily routine in fair comfort even though the bruit is still faintly audible with the stethoscope, but the lesion cannot be considered absolutely cured until the fistulous opening is closed. The lesion tends to be progressive and will recur unless the fistula is closed, or the involved vessel is isolated from the general circulation.

All spontaneous cures of these fistulas have been by thrombosis, vision of the ipsilateral eye being lost. The majority of patients having this lesion are blind from the outset, and blindness practically always results from later thrombosis of the cavernous sinus. Any method of treatment that requires thrombosis will result in a high incidence of blindness. If retrograde flow can be induced through the branches of the ophthalmic artery and vein from their external carotid anastomoses, it might be possible to ligate these vessels proximal to their branches (fig. 2 *e*) and establish an entirely new ophthalmic circulation. This probably would save the eye.

7. Dorrance, G. M.: The Operative Treatment of Pulsating Exophthalmos, Am. J. Ophth. **13**:675, 1930.

Before operating on these patients by any method, a period of preliminary carotid compression must be instituted for the purpose of encouraging collateral circulation through the circle of Willis and to accustom the ipsilateral cerebral hemisphere to changes in arterial blood pressure. By this procedure the incidence of hemiplegia has been greatly reduced. At first the patient may not be able to stand more than one or two minutes of compression before feeling dizzy or faint. Compression is promptly stopped, but is repeated in increasing lengths of time, every three hours, until the patient can bear from thirty to forty-five minutes of occlusion without signs of cerebral damage. The pulsations of the carotid are felt; then the artery is pressed backward and inward against the transverse processes of the lower cervical vertebrae. The bruit should be listened for to determine whether or nót occlusion is complete. While various mechanical devices have been designed for this purpose, digital compression is probably the most reliable.

Two cases are presented demonstrating the application of several combinations of the previously outlined principles of treatment.

REPORT OF CASES

CASE 1.[8]—A woman, aged 32, entered the clinic on April 17, 1931, complaining of blindness in the right eye, protrusion of the eye and a constant swishing roar in the head synchronous with the pulse. On Feb. 6, 1931, she had received a severe blow on the right supra-orbital area in an automobile accident, the lacerations caused by this requiring suture. She immediately became unconscious and remained so for six days. On regaining consciousness, she was blind in the right eye, and a roaring noise was heard, which had been present constantly since. Hearing was diminished on the right side, and the patient was dizzy.

Examination revealed a right pulsating exophthalmos with a systolic bruit and blindness. There was a palsy of the sixth nerve on the right side, and the pupils were irregular, the right being larger than the left. The left pupil reacted to light and in accommodation normally; the right consensually only. The palpebral fissures measured 11 mm. on the right and 8 mm. on the left. There was a severe degree of conjunctival edema in the right eye with engorgement of the retinal vessels and atrophy of the optic disk. The only other finding of significance was a positive Romberg sign.

Lumbar puncture revealed an initial pressure of 110 mm. of water, a normal response to Queckenstedt's test and clear, colorless fluid. The spinal fluid showed a faint trace of globulin, with a colloidal gold curve of 5555521000; the Wassermann and Kahn reactions were 4 plus; the total protein was 30 mg. per hundred cubic centimeters of fluid. The Wassermann reaction of the blood was 4 plus in three antigens, and the Kahn reaction, 2 plus.

A roentgenogram of the right orbit showed erosion of the superior inner margin of the orbit. Other laboratory tests gave normal findings.

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8. This case was reported originally in the Cleveland Clinic Quarterly (A Case of Traumatic Retrobulbar Arteriovenous Aneurysm, January, 1932, vol. 1, no. 1).

The patient was started on antisyphilitic treatment. It was found that digital compression of the right common carotid artery against the carotid tubercle made the patient dizzy and weak after two or three minutes, but it stopped the roar in her head and stopped the pulsation of the exophthalmos. To accustom her to diminished blood supply through the cerebral arterial system, digital compression was applied to the artery several times daily until, twenty-five days after she entered the hospital, she could tolerate compression for twenty-five minutes with ease.

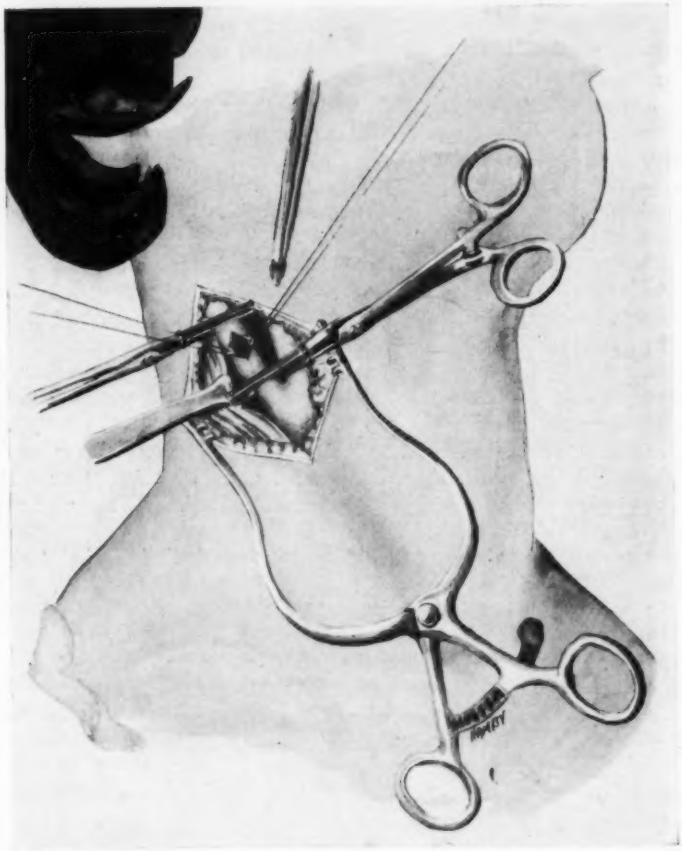

Fig. 4.—An insertion of muscle plug into internal carotid artery.

It was decided to attempt a direct occlusion of the fistula by the method of Dr. Brooks.

On May 15, the patient was operated on (fig. 4). Under local anesthesia, a 3 inch (7.6 cm.) incision was made just in front of the anterior border of the sternocleidomastoid muscle on a level with the thyroid cartilage. The common carotid artery with its bifurcation was exposed. Compression of the external carotid did not affect the bruit, while compression of the internal carotid stopped it completely. The internal carotid was then dissected free for a distance of 4 cm. and was clamped with two rubber-shod artery clamps. A vertical incision about 1 cm. long was made into the lumen of the artery between the clamps. A purse-

string suture of silk was placed around the incision, after which a piece of muscle was removed from the platysma, cut to the size of a pea and clamped with a small silver hemostatic clip. This was tucked into the opening in the artery. The purse-string suture was tied and was oversewed with two additional running silk sutures. The clamps were removed and the artery replaced in its bed. The patient noticed no recurrence of bruit following the removal of the clamps, which had been left on for about twenty minutes with no untoward effects. A tape treated with petrolatum was put around the internal carotid artery to allow for traction hemostasis in the event that the arterial sutures failed to hold. This was removed twenty-four hours later. The wound was closed with buried silk and with clips to the skin. The patient's condition and morale were excellent throughout.

Roentgenograms showed the silver clip which had been attached to the muscle embolus to be in the right side of the skull just to the outer side of the dorsum sellae and on a level with its floor (fig. 5).

The patient was kept in bed, and quiet was strictly enforced. She complained of headache and had some emesis for two days, probably the result of the changes in cerebral blood flow.

On the third day, a thrombus was palpable in the upper lid, and chemosis of the conjunctiva was becoming prominent. On the sixth postoperative day, a bruit became audible with the stethoscope, but it was much less than it had been a week previously. The patient had not heard the bruit since the operation.

On July 8 (fifty-three days after operation), the patient was readmitted to the hospital. Her progress had been excellent, but the bruit had become audible to the patient a short time before.

On examination, the right eye looked much better, not so large or injected. The palpebral fissure on the right was 9 mm., wider by 1 mm. than on the left. There was almost complete atrophy of the right disk. The bruit was audible, but there was no palpable thrill.

In this case, the muscle plug and subsequent thrombosis had almost obliterated the fistula. Knowing the progressive nature of these lesions, it was decided further to diminish the blood supply with the hope of obtaining a complete cure.

On July 9, under gas and local anesthesia, the right common and internal carotid arteries were ligated. The patient progressed very satisfactorily. She had some headache at times, but the bruit was inaudible at all times. She was discharged on July 17. She has continued antisyphilitic treatment intermittently, since she is living away from medical attention and is not able to get to a physician often.

We last saw her on April 7, 1932. At that time there was no audible bruit. There was absolute atrophy of the right disk, and the difference in the width of the palpebral fissures was 1.5 mm. Her condition was excellent, and she had no complaints.

The second case of pulsating exophthalmos proved interesting on account of the rapid development of anastomoses after ligation of the vessels.

CASE 2.—A rather obese woman, aged 48, was first seen at Charity Hospital on Sept. 27, 1931. She had fallen from a balcony thirteen weeks before, striking her head on a concrete sidewalk, and had been rendered unconscious. She had remained in that state, or semiconscious, for three days. Roentgenograms disclosed a linear fracture of the right frontal region. On regaining consciousness, she had been aware of a "rushing," throbbing sound on the left side of the head. The right eye, which had been greatly congested and discolored at first, rapidly improved.

There was no extra-ocular palsy at that time. As convalescence progressed, vision in the left eye began to fail, conjunctival edema and protrusion of the left eye developed, and she had severe headache.

Examination disclosed marked venous congestion of the left conjunctiva and lids and marked left conjunctival chemosis. There was a loud bruit over the left eye, synchronous with the pulse. This could be controlled entirely by compression of the left common carotid artery. There was complete paralysis of the left sixth

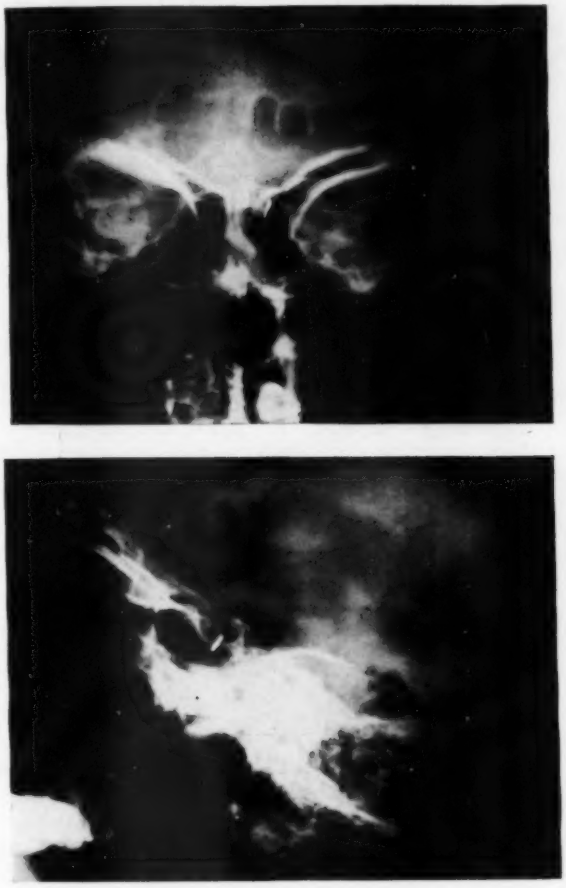

Fig. 5.—Roentgenograms of skull, showing clip in place. Upper picture, anterior view; lower picture, lateral view.

nerve and partial paralysis of the third and fourth nerves. There was some hypalgesia over the area of distribution of the first division of the left fifth nerve. The other cranial nerves functioned normally.

The diagnosis was pulsating exophthalmos, with the fistula between the internal carotid artery and the cavernous sinus, and paresis of the left second, third, fourth, fifth and sixth nerves.

To accustom the patient to diminished cerebral blood supply and to allow the other vessels to compensate, digital carotid compression was applied every three hours, starting with one minute, then increasing as rapidly as possible. She became

able to stand thirty minutes of compression without discomfort. It was then proposed to insert a muscle embolus into the artery as in the previous case.

Operation was performed on October 9 at Charity Hospital. The left internal carotid artery was exposed, elevated and compressed, and the bruit was controlled completely. The artery was dissected for a distance of 3 cm., and a rubber-shod artery clamp was placed at each end of this area. Owing to technical difficulties, however, the attempt to insert a muscle embolus was unsuccessful, so the vessel was ligated and cut. The common carotid was exposed and ligated below its bifurcation, and the incision was closed. A pressure bandage was applied to the eye for twenty-four hours. The bruit was still faintly audible with the stethoscope, but was not heard subjectively.

Eighteen days later, auscultation disclosed a faint bruit, although the patient was not conscious of its presence. There were still paralysis of the left sixth nerve

Fig. 6.—Intracranial ligation of left internal carotid artery. Frontal lobe retracted; ligature around internal carotid artery.

and paresis of the third nerve. Exophthalmos had cleared up, chemosis had disappeared, and there was no palpable thrill. A thrombus was palpable in an orbital vessel just above the outer canthus.

The patient was readmitted to the hospital on March 30, 1932, four and one-half months after the first operation. She had been well since her last visit, but the headache had been increasing in severity, and vision was failing at times in the left eye, although frequently it was better than in the right. The bruit was audible subjectively at intervals.

Examination disclosed that the patient had lost some weight, but she looked much better. There were moderate dilatation and congestion of the left scleral vessels, but no thrombosis; they could be emptied by pressure. The two eyes were of about the same size. There was a loud bruit in the left eye, in the left frontal and maxillary regions and, to a lesser extent, over the right globe. Pressure on the right carotid failed to stop the bruit.

Examination showed a normal right fundus, while the left showed marked tortuosity of the retinal vessels with a small amount of papilledema. The visual fields were full.

The bruit following the ligation of the left carotid artery came, of course, from retrograde blood flow through the circle of Willis and down into the injured vessel. This flow could be controlled at first by shutting off the right carotid flow. The vertebral and basilar arteries later enlarged, until they were transmitting enough blood to cause bruit without the carotid contribution. It was proposed, then, to ligate the artery intracranially between the cavernous sinus and the circle of Willis.

On March 31, an encephalogram was taken for the dual purpose of draining the cerebrospinal fluid and of determining the amount of cerebral damage resulting from trauma and the lesion. The plates disclosed only traumatic pia-arachnoid adhesions over the right cerebral hemisphere.

On March 31, a left frontal craniotomy was performed as for an approach to the sellar region. The left internal carotid artery was ligated with a double silk ligature just above the cavernous sinus, leaving the circle of Willis intact. Following the operation, no bruit was audible in either eye. The next morning, however, the bruit was audible faintly both subjectively and objectively over both eyes. Pressure on the right carotid artery controlled it completely. The recurrence of the bruit was a great disappointment, of course, but since these lesions are known to be progressive rather than tending to cure, it was felt that further intervention should be attempted.

Within the sinus, the internal carotid artery gives off one large vessel, the ophthalmic, and several minute twigs, one of which anastomoses with the middle meningeal, the others supplying the pituitary gland. Since the ophthalmic is the largest of these, it was reasonable to assume that its anastomoses were responsible for the retrograde flow. Several operators (Hanford and Wheeler) have ligated the ophthalmic artery and vein within the orbit as a part of their attack on these lesions. The ophthalmic anastomoses with the external carotids through a number of branches, the most important being the supra-orbitals and infra-orbitals and the ethmoid. The left external carotid was already occluded. All these other anastomoses were supplied by the opposite external carotid. A period of daily right carotid compression was then started, and finally the patient could tolerate, with ease, pressure for thirty minutes every three hours.

On April 11, fourteen days after the craniotomy, the right common artery and the internal and external carotid arteries were ligated at the area of bifurcation. This procedure stopped all bruit, objective and subjective, and the patient had no further complaints except an occasional slight headache. She was allowed out of bed six days after operation; she had no dizziness or other cerebral symptoms and was discharged on April 23, twelve days after ligation of the right carotid artery and twenty-three days after craniotomy.

COMMENT

Unfortunately, most of us see so few of these cases that each is a new experience when it confronts us. It is obvious, however, that the "routine" treatment by ligation of a carotid artery is inadequate completely to cure this lesion and that rational, effective treatment is yet to be determined. These cases demonstrate that such a progressive lesion often requires a progressive attack, and that it should be energetically dealt with until such a time as a successful outcome seems assured.

SURGICAL ASPECTS OF RENAL AGENESIS

WITH SPECIAL REFERENCE TO HYPOPLASTIC KIDNEY, RENAL APLASIA AND CONGENITAL ABSENCE OF ONE KIDNEY

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NEW YORK

Among the most enigmatic surgical anomalies of the upper urinary tract which interest the medical profession and particularly the surgical specialist are the three much confused borderline conditions of hypoplastic kidney, renal aplasia and congenital absence of one kidney. All of these have clinically the same common denominator, in that when the supposedly sound kidney is removed at operation for an associated pathologic process, the outcome is promptly and inevitably anuria and death. But fortunately, the time has come when these three very hazardous and unrecognized conditions of the past can be differentiated and accurately identified before postmortem examination.

A survey of the literature on this rather obscure subject reveals that the underlying cause of such a compromising situation is an embryonic malformation and lack of proper development of the urinary organs, which is also commonly associated with developmental defects of the genital organs. The problem is further confused by lack of proper classification, due to failure to recognize many of these cases and to the impossibility of obtaining sufficient clinical data. Many authors who have written on this subject have not had a clear conception of these three unusual conditions and have often confused them with a secondary or acquired type of atrophy of the kidney, when in reality one is dealing with an arrest of development of the organ. A solitary kidney or atrophy of one kidney has been rather commonly found at postmortem examination. Various authors, in reporting a long series of autopsies totaling 92,690, give the relative frequency of hypoplastic kidney as 1 in 600, that of renal aplasia as 1 in 400 and that of solitary kidney as 1 in 1,600. The clinical ratio has never been accurately established, because, prior to the era of cystoscopy and pyelography, the preopera-

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tive or antemortem diagnosis was seldom made; consequently, the cases found at operation or on the dissecting table have been surprisingly numerous. It is necessary at this time to specify that in this study I shall not discuss the condition recorded by many authors as congenital or acquired atrophy of the kidney, when the atrophy is due to disease, trauma or an associated pathologic process in which the kidney undergoes complete destruction, losing its renal parenchyma and becoming functionless, as commonly occurs in tuberculosis, hydronephrosis, pyonephrosis or stone long impacted in the ureter. In this paper I shall deal exclusively with the variety of congenital malformation in which one kidney is absent, or there is a rudimentary or infantile type of kidney, or an arrest occurs in the development of the organ, which is consequently incapacitated to sustain life. It is obvious that while this condition is of clinical interest to the embryologist and pathologist, it is of even greater importance to the urologist and the surgeon. The only lesion with which I am concerned in this study is the unilateral type, since when the condition is bilateral it has no clinical interest, in that it is at the outset incompatible with life.

The best conception of this malformation of the upper urinary tract is that it represents an embryonic defect or lack of development during intra-uterine life, when the organ in its evolution did not develop to its full extent or the wolffian duct of the mesonephros failed to produce a renal bud after the duct had reached the cloaca, as in the case of unilateral renal agenesis. The variation in the evolution and mechanism of the migration, ascent and rotation that these organs undergo from their position in the bony pelvis behind the cloaca to the lumbar region in the adult explains the multiplicity of variations of congenital malformations that may be encountered. In studying the surgical aspect of congenital anomalies of the kidney, one cannot fail to be tremendously impressed with their frequency, particularly in a routine urologic practice, since they constitute about 40 per cent of all pathologic lesions of the kidney. Hence proper clinical recognition is of extreme value, not only for establishing a correct diagnosis but also to assure a sound prognosis.

In reporting eight cases to illustrate these three varieties of renal agenesis, which I have had the opportunity to study at the urological department (James Buchanan Brady Foundation) of the New York Hospital, I shall discuss first the most important points in the preoperative diagnosis. Secondly, I shall emphasize the value of a complete and careful urologic and urographic examination in order to avoid the dangerous surprise that is involved in this renal hypoplastic, or aplastic, or agenetic condition. It is also my purpose to point out the surgical aspect of this problem and its proper treatment.

Since it is obvious that the borderline differentiation between these three clinicopathologic conditions of the kidneys has not been mentioned

in any textbooks, and since this is indeed not easily recognized, the problem it presents is often not adequately solved. It seems proper, therefore, to study the three conditions separately, while describing the illustrative cases of each modality. In an attempt to abbreviate this communication and to make it of more practical interest, I have summarized its main points in the following tabulation, basing my classifications on the most important clinicopathologic and cysto-uropyelographic data as a means of differentiating these three unique conditions of the undeveloped kidney. The three descriptive classifications which I have worked out with a view to facilitating a correct diagnosis will serve to establish greater accuracy in their clinical and anatomopathologic description and their proper differentiation.

Classification and Clinicopathologic Differentiation of Hypoplastic Kidney, Renal Aplasia and Congenital Absence of One Kidney

Hypoplastic Kidney

1. Small or infantile in type; other kidney hypertrophic
2. Normal renal parenchyma
   (*a*) With medullary and cortical substance
   (*b*) With absence of pyramidal substance
3. Microscopic sections reveal normal or rudimentary glomeruli and tubules
4. Rudimentary or hydronephrotic pelvis
5. Calices bizarre in position and size, sometimes absent
6. Patent ureter
7. Normal urine secretion
8. Diminished or normal renal function
9. Good urea excretion and phenolsulphonphthalein elimination
10. Pyelography and roentgenography reveal hypoplastic kidney or diminutive organ

Renal Aplasia

1. No true kidney
2. No evidence of pelvis
3. Absence of true renal pedicle
4. Renal artery small or absent
5. Ureter incompletely developed and not patent
6. No excretion of urine
7. No renal function
8. Bladder with two normal ureteral orifices or one ectopic ureter
9. Histologic section of the supposed renal mass reveals glomeruli and tubules, showing arrest of development of renal organ
10. Cystoscopy, catheterization of ureters and descending or ascending pyelography for diagnosis of the condition

Congenital Abscence of One Kidney (Congenital Solitary Single Kidney)

1. No evidence of hypoplastic or aplastic renal tissue
2. Complete absence of a mate with hypertrophy of the solitary kidney
3. Single kidney with double pelves and double ureters, or
4. Kidney with single or double ureters in cross ectopia

5. Vesical trigone distorted or absent
6. Bladder with one ureter or two openings in one side
7. Suprarenal nearly always absent
8. About 70 per cent of the cases of solitary kidney found with some other type of congenital malformation, particularly of the genital tract
9. Diagnosis obtained cystoscopically and pyelographically by the descending or ascending urographic method

HYPOPLASTIC KIDNEY

Unilateral renal hypoplasia is that condition in which a kidney that is apparently well developed anatomically and histologically is diminutive, fetal or infantile in size, or hypoplastic or defectively developed. While apparently having good secretory function in regard to elimination of urea and of color dye, the organ does not have enough capacity for undergoing functional hypertrophy to sustain life. Chopart,[1] Morgagni,[2] Cruveilhier,[3] Sappey,[4] Testut,[5] Rayer[6] and other earlier anatomists knew that one kidney might be large and the other small, but these observers did not differentiate congenital or primary hypoplasia from sclerotic, inflammatory and other forms of secondary contractions of atrophy. Indeed, the term atrophy, so frequently used in the literature, misleads in the conception and proper understanding of the condition, because these kidneys have at no time been larger than when found. Hence it is a condition of renal disparity, and many authors have described it as a rudimentary or infantile organ. There is an arrest in its development and not an atrophy. Gastaldi,[7] who reported sixty-six cases in his thesis, had the same idea, and termed it an inequality of renal volume, but did not differentiate the type of hypoplastic kidney from that of renal aplasia and total agenesis. Cadoré[8] and Gerard,[9] in classifying the congenital anomalies of the kidney, included "relative atrophy," obviously meaning abnormal smallness of one kidney, and applied the term "absolute atrophy" to a more

1. Chopart: Traité des maladies des voies urinaires, Paris, 1821.
2. Morgagni: De sedibus et causis morborum, Leyden, C. Haak, 1765. Letter XXXI, art. 25; XLVIII, art. 16.
3. Cruveilhier, Jean: Traité d'anatomie pathologique, Paris, J. B. Baillière et fils, 1849.
4. Sappey, M. P. C.: Traité d'anatomie descriptive, Paris, V. Masson, 1850.
5. Testut, Jean: Tratado de anatomi humana, Barcelona, Salvat y Ca, vol. 4, p. 478.
6. Rayer: Traité des maladies des reins, Paris, J. B. Baillière, 1841. See also his Atlas, 1837.
7. Gastaldi, M.: Contribution à l'étude de l'inégalité du volume des reins et de l'atrophie congénitale unilatérale, Thèse de Paris, 1910.
8. Cadoré, F. L.: Les anomalies congénitales du rein chez l'homme, Thèse de Lille, 1903, no. 144.
9. Gerard: Les anomalies congénitales du rein, J. de l'anat. et physiol. **41**:241 and 411, 1905.

marked lesion. Teyssèdre,[10] in his thesis, used the term renal agenesis, and Polack[11] also described and classified the condition as agenesis, distinguishing a relative and an absolute type. In more recent literature, Albarran,[12] Marion,[13] Papin,[14] and Eisendrath and his co-workers[15] classified this condition more properly as hypoplasia, while McArthur,[16] Geraghty and Plaggemeyer[17] and other writers described it as the infantile kidney. Coplin[18] emphasized the condition of unilateral hypoplasia, explaining the possibilities of defective arteriogenesis in relation to the so-called hypogenetic nephritis. Astraldi[19] and Papin and Verliac[20] of the Necker Clinic also more recently stressed the congenital origin of this malformation as well as the concomitant anomalies of the genital tract, and reported a case in which the patent ureter of the hypoplastic kidney opened into a seminal vesicle.

However, the borderline between hypoplastic kidney and renal aplasia has not, on the whole, been well established, either clinically or histologically, since most of the pathologists include this recognized type of lesion under unilateral congenital or acquired atrophic kidney, as if it were due to an associated pathologic process. In 1902, Albarran[12] was among the first to call attention to the danger of this hypoplastic kidney, reporting a case in which, with good elimination of urea and of color dye, and apparently good concentration of the chemical

10. Teyssèdre, Emile: Contribution à l'étude des anomalies de développement du rein, Thèse de Paris, 1892, no. 370.

11. Polack, Lazare: Contribution à l'étude des agénésies rénales, Thèse de Bordeaux, 1909, no. 64.

12. Albarran, Joaquin: Exploration des fonctions des reins: Etude médico-chirurgical, Paris, Masson et Cie, 1905.

13. Marion, G.: Traité d'urologie, Paris, Masson et Cie, 1928, p. 418; Hypoplasie rénale, discussion, Bull. Soc. franç. d'urol., séance du 17 mars, 1930, p. 50. Legueu: Hypoplasie rénale, discussion, Bull. Soc. franç. d'urol., séance du 17 février, 1930, p. 62. Chevassu: L'hypoplasie rénale, discussion, Bull. Soc. franç. d'urol., séance du 17 février, 1930, p. 62 .

14. Papin, Edmond: Anomalies congénitales du rein, Encyclopédie française d'urologie, Paris, Doin et fils, 1914, vol. 3, p. 227. Verliac, Papin and Astraldi: L'hypoplasie rénale, Bull. Soc. franç. d'urol., Feb. 17, 1930, no. 2, p. 56.

15. Eisendrath, D. N., and Rolnick, H. C.: Textbook of Urology, ed. 2, Philadelphia, J. B. Lippincott Company, 1930, p. 575. Papin and Eisendrath: Les anomalies des reins et des urétères, Arch. d. mal. d. reins **2**:421, 1926.

16. McArthur, L. L.: Surg., Gynec. & Obst. **12**:391, 1911.

17. Geraghty, J. T., and Plaggemeyer, H. W.: The Practical Importance of Infantile Kidney in Renal Diagnosis, J. A. M. A. **61**:2224 (Dec. 20) 1913.

18. Coplin: Unilateral Renal Hypoplasia and Dysplasia, Am. J. M. Sc. **153**: 381, 1917.

19. Astraldi, A.: Hypoplasie rénale congénitale, Arch. urol. de clin. de Necker **7**:47, 1931.

20. Papin and Verliac: Hypoplasie rénale congénitale avec abouchement de l'urétère dans la vésicule séminale, J. d'urol. **1**:431, 1920.

elements of the urine, he did a nephrectomy for renal tuberculosis, and eleven days later the patient died in a uremic coma. When the autopsy revealed a congenital hypoplastic or infantile type of kidney, he concluded that the hypoplastic kidney is incapable of undergoing compensatory hypertrophy after nephrectomy. Also, McArthur,[16] in 1911, reported another case in which he had performed a nephrectomy for tuberculous pyonephrosis, which was followed by death from renal insufficiency; at necropsy a tiny, infantile kidney, with normal parenchyma and normal secretion of urine, was found, but again the capacity for functional hypertrophy was lacking.

More recently, another author,[21] in a study on renal anomalies, reported an illustrative case of this type, in which, with good excretion of indigo carmine from both ureters and a positive pyelogram revealing an infected hydronephrosis, nephrectomy was done; four days later the patient had passed only 2 ounces of bloody urine and died with the typical symptoms of uremic poisoning; at autopsy, the left kidney was found to be of the hypoplastic type.

Geraghty and Plaggemeyer,[17] calling attention to the difficulty and importance of recognizing this so-called infantile kidney, reported on a study of 3,940 necropsies from the Johns Hopkins Hospital, among which they found 36 cases of atrophy from various causes; they stated that of these only 6 were unilateral, and that of the 6, only 3 belonged to the infantile or hypoplastic type; they further stated that there is much greater risk involved with a deficient kidney of the infantile type than with any other type of renal agenesis. All the statistics in this respect, therefore, are most confusing, because of the lack of differentiation and proper classification. In the future, however, these diminutive kidneys should be better known and properly recognized clinically, when careful routine urologic and urographic examinations are made.

The hypoplastic kidney, as a rule, is from three to six times smaller than the one of the opposite side, which is always hypertrophic. Two types may be described: In the first, the architecture of the renal parenchyma is normal with a normal pelvis and ureter, although the pelvis is of pear form or bottle shape and diminutive; the calices are also very small and sometimes unusually placed or anatomically disoriented. The second type is that in which the medullary portion and the pyramids are absent, and, therefore, there is only cortical substance and the pelvis may be of hydronephrotic type, as in Marion's case and in one of the cases that I am here reporting. In some of these cases the microscopic study reveals rudimentary glomeruli and tubules. In others the tissue resembles that of a normal kidney but is present in minimal amount. I am reporting two such cases that have been correctly diagnosed clinically and which were confirmed at operation, as

21. Magoun, J. A. H.: Renal Anomalies, J. Urol. **27**:435 (April) 1932.

can be seen in the report of the case. The chief diagnostic sign in hypoplastic kidney is marked decrease in function, both quantitatively and qualitatively, with reference to excretion of urea and elimination of color dye in comparison with that of the opposite side when the latter is normally and fully developed. But when the kidney of the opposite side is suffering from some type of associated pathologic process, the secretory function of both organs is affected and definitely diminished. Hence, the differentiation necessary to establish a correct diagnosis depends on the interpretation of the bilateral pyelogram combined with

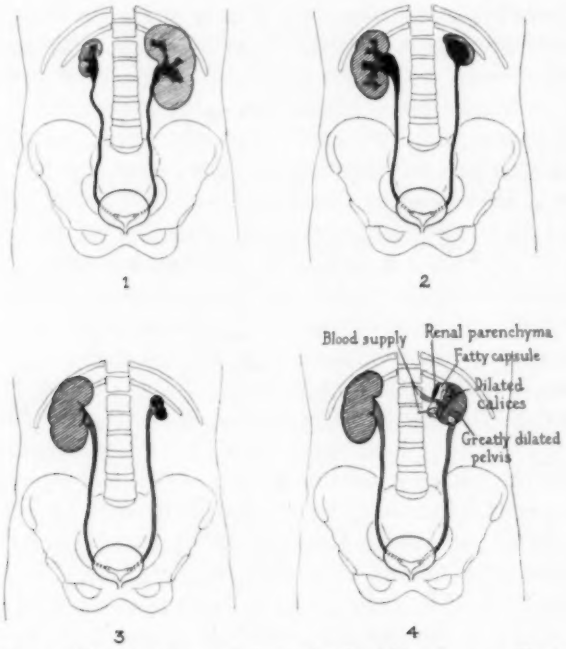


Fig. 1.—The different types of hypoplastic kidney, as collected from the literature: *1*, author's case, representing a typical right hypoplastic kidney with marked hypertrophy of the left kidney; *2*, a left hypoplastic kidney in which only cortical substance is present with no evidence of calices, papillae or pyramids; *3*, a diminutive hypoplastic kidney with rudimentary pelvis and patent ureter; *4*, marked hydronephrosis in an extremely hypoplastic kidney in which patency of the ureter and renal function are present. Note that in the hypoplastic kidney the ureter is always patent and there is evidence of some renal function.

the shadow cast and outline of the kidney obtained in a good x-ray plate, in which the size and position of both organs can be accurately made out. The pyelographic and roentgenographic evidence furnished by the outline of the kidney, which may be very small with extremely small pelvis and with calices absent or rudimentary, in contrast with hypertrophy of the opposite normal kidney, will serve to verify the diagnosis.

With this congenital malformation of hypoplastic kidney in mind, the advisability of taking a bilateral pyelogram in order to detect this condition is beyond all question. In the future, many of these cases may be clinically recognized through the facility with which the method of intravenous pyelography can be used. Nevertheless, in many of these cases, when the intravenous injection of iopax for the purpose of finding out the condition of the kidney is employed, and the opaque substance is not sufficiently concentrated or eliminated by the kidneys, and is therefore not well visualized, it will always be necessary, and perhaps safer, in order to establish a correct diagnosis, to use the ascending method of taking ureteropyelograms for the purpose of verifying a suspected condition and revealing the presence of a hypoplastic kidney.

REPORT OF CASES

CASE 1.—*Nephrectomy for hypoplastic kidney.*

Mrs. L. H., a housewife, aged 26, came to the Brady Urological Clinic of the New York Hospital on Oct. 31, 1930, complaining of pain in the right lumbar region with slight frequency of urination day and night, and also dysuria and pyuria. The pain in the lumbar region and upper right quadrant had been intermittent since she was 9 years of age. This pain lasted for four or five days and disappeared. She also had pain in the left lumbar region. Cystoscopy had been performed elsewhere and a diagnosis of pyelitis and pyelonephritis made, but no treatment had had any effect on her condition. The left kidney was enlarged and tender on palpation. The right kidney was not palpable, but there was pain in the right upper quadrant on deep palpation. Although well developed, the patient was of feeble constitution, but had a 6 year old child living and well. Aside from the fact that her menstrual history had always been painful and irregular, no other abnormalities were made out.

On November 3, cystoscopy was performed and both ureters were catheterized; a differential renal test revealed that function of the right kidney was much diminished in comparison with that of the left. The culture also revealed Bacilli coli-communis from the right ureter and bladder, while culture from the left was negative. Also, microscopic examination of the wet specimen revealed two white blood cells per field, while from the left side there was no pus.

On November 13, cystoscopy was again performed and bilateral pyelograms were taken. The roentgen report on the genito-urinary tract revealed that the shadow of the left kidney was considerably enlarged; and while the shadow of the right kidney was not clearly seen, there was no shadow indicative of stone anywhere in the urinary tract. The pyelogram of the right kidney revealed a small elongated bottle-shaped pelvis of infantile type, showing diminutive calices and some dilatation of the upper calices; also some distortion of the ureter was seen, and the impression was that of a hypoplastic organ which had not been fully developed (fig. 2). The pyelogram of the left kidney showed a slightly dilated pelvis with dilatation of the major and minor calices; it also revealed that the left kidney was about four times larger than the right, and that apparently this hypertrophic organ was carrying on in a compensatory manner the function of its mate. With this finding, cystoscopy was again performed on November 24, at which time the specimen collected from both sides was sent to the laboratory for inoculation into a guinea-pig in order to rule out the possibility of tuberculous infection. At the

same time, in the routine treatment, each kidney was irrigated with a solution of dextrose containing an acridine derivative and a bougie no. 8 was passed to each renal pelvis to dilate the ureters, to correct infection and to assure better drainage. To ascertain the differential function and to determine whether nephrectomy of the infantile organ was indicated, the functional test was repeated. One week later, December 1, when cytoscopy was again performed, the differential functional test was made.

The specimen of urine from the right ureter was bloody and contained 0.5 Gm. of urea per liter; that from the left ureter was clear and contained 4 Gm. of urea per liter.

The phenolsulphonphthalein test gave the following results: time of appearance from the right ureter, five minutes; per cent of phenolsulphonphthalein, 1.5; time of collecting, ten minutes; time of appearance from the left ureter, two minutes; per cent of phenolsulphonphthalein, 9; time of collecting, ten minutes.

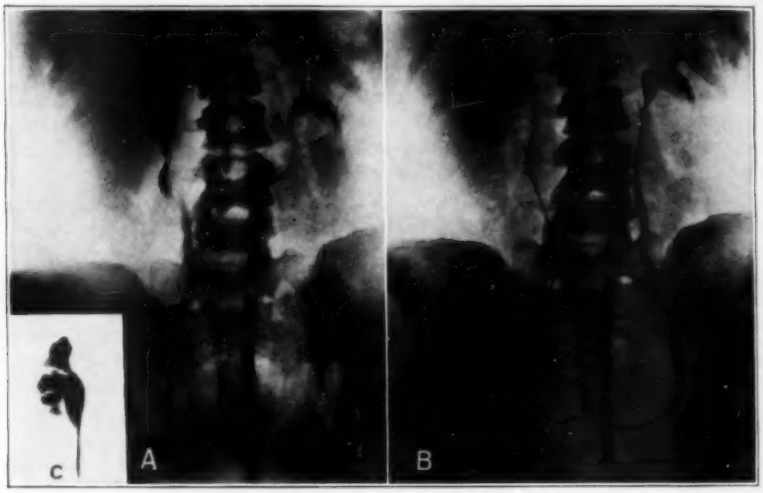


Fig. 2 (case 1).—*A*, bilateral pyelo-ureterogram, revealing a typical picture of a right hypoplastic kidney with a very diminutive pelvis and a slight dilatation of the upper calix. There can also be seen the rudimentary lower and middle calices, and a faint shadow of the outline of the diminutive organ. *B*, pyelo-ureterogram of the left kidney from the same case, revealing an enormous kidney shadow with a normal pelvis as the expression of a compensatory functional hypertrophy. *C*, pyelogram of the specimen removed at operation, revealing the diminutive type of infantile hypoplastic kidney.

Microscopic examination of the sediment of the wet specimen from the right ureter showed 1 epithelial cell, 6 red blood cells and 2 white blood cells per high power field. The specimen from the left ureter showed 3 epithelial cells per high power field, much detritus and crystals.

Culture of urine from the right ureter showed B. coli-communis; the urine from the left ureter was normal, and that from the bladder contained B. coli-communis.

The conclusion was, therefore, that the patient was suffering from a faulty development of the right kidney, the so-called infantile kidney, having practically

no function and associated with pyelitis and pyelonephritis. In view of this, she was admitted to the hospital and nephrectomy was done under spinal anesthesia on Jan. 20, 1931.

I found at operation that the kidney was very easily exposed by the lumbar oblique incision, and that there was little perirenal fat present. On opening the fatty capsule, the kidney was found to be of infantile aspect and extremely small. The ureter was easily separated and ligated. The renal pedicle of the kidney, which was also seen to be very small or atrophic, was likewise easily dissected free from the surrounding tissues, clamped and tied, and the kidney was removed,

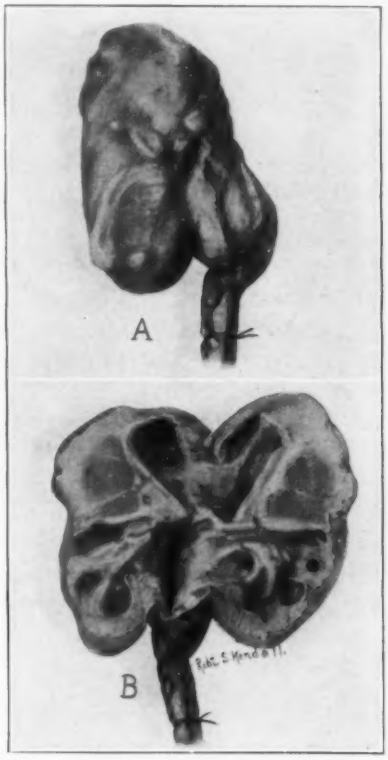


Fig. 3 (case 1).—Drawing of the specimen removed at operation: *A*, the anterior aspect of the diminutive kidney; *B*, sagittal view, laid open, of the infantile hypoplastic kidney, revealing slight dilatation of the upper calix and a slight degree of hydronephrosis. Note that the parenchyma of the kidney is composed of medullary and cortical substance, and also that the excretory apparatus is very diminutive and hence incapable of undergoing compensatory hypertrophy.

this constituting one of the simplest and easiest nephrectomies I have ever encountered. Recovery was uneventful, and the patient left the hospital in good condition two weeks later.

The specimen removed at operation revealed the presence of a hypoplastic type of kidney, associated with pyelitis and pyelonephritis. A pyelogram was made of the specimen removed at operation (fig. 2 *C*); it showed a small amount of renal

parenchyma and a tiny infantile type of pelvis, which obviously corresponded with the pyelogram taken before the operation, thus giving full evidence of the correctness of the diagnosis.

Macroscopically, the specimen was a diminutive or infantile organ with a slight degree of hydronephrosis (fig. 3). On cutting the specimen in half the medullary and cortical substances were found to be within normal limits. The architecture of the organ was also quite normal, except that it was diminutive in type and that some of the pyramids and calices as well as the papillae were distorted owing to the association of slight hydronephrosis with pyelitis and pyelopnehritis. However, the ureter and ureteric-pelvic junction were within normal limits and truly patent.

The histologic report of the specimen was as follows: The specimen consisted of a kidney measuring 7 by 4 by 2.5 cm. The microscopic sections showed marked scarring of the cortex within large portions, disappearance of the glomeruli, dilatation or atrophy of the tubules, increased fibrous stroma and thickening of the arterioles with diminution of their lumina. The pelvic mucosa was heavily infiltrated by lymphocytes. The covering epithelium was not well preserved. In some of the thicker parts of the kidney more normal appearing glomeruli and tubules were seen, but even here there were streaks of scarring with varying stages of thickening of Bowman's capsule and fibrosis of glomeruli.

The conclusion to be drawn from this case is that the clinical evidence may be misleading for the diagnosis, since this hypoplastic or infantile type of kidney has a certain amount of function in regard to elimination of urea and color dye, and the chemical elements of the urine may be normal. But when anuria sets in, or nephrectomy is done for an associated pathologic process in its mate, this fetal type of kidney is incapable of undergoing hypertrophy. This therefore brings out the fact that in this diminutive type of pelvis the dynamism of the emptying time is affected in two ways: first, by the retention and lack of excretory elimination and, secondly, by the development of urinary stasis, which will ultimately lead to hydronephrosis, pyelitis and pyelonephritis. The diagnosis is made urographically, and two groups of cases must be considered: first, the type herein described of a hypoplastic organ with hypertrophy of its mate, when nephrectomy of the diminutive kidney is the proper indication, and, secondly, the type in which the hypertrophic organ is the one suffering from the associated pathologic process, while the infantile kidney of the opposite side is executing a certain amount of function but not enough to sustain life when left alone. In this case the hypertrophic kidney should be given the most careful treatment, such as one would accord in cases of a single kidney when conservative surgical and urologic therapy is the only proper indication.

This patient was examined just one year after her operation. She has gained in weight and is free at the present time from urinary symptoms. This case shows how these conditions can be accurately diagnosed today by the routine method of investigation, with both the differential renal functional test and the urographic data.

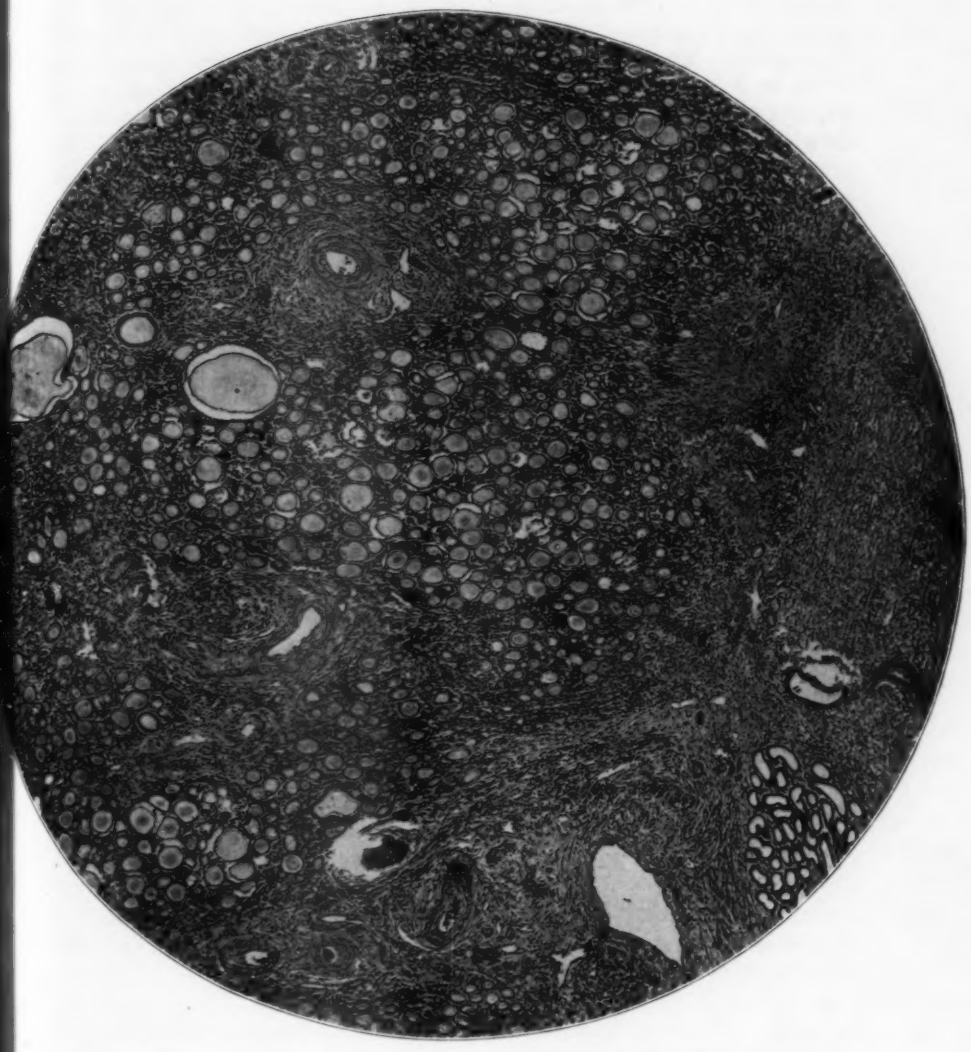


Fig. 4 (case 1).—Photomicrograph of section made from the removed specimen, revealing embryonic type of tubules, hyalinization of glomeruli and marked sclerosis of the blood vessels. Note the degeneration of tubules with flattening of the epithelium and dilatation of tubules and glomeruli to the extent of cyst formation. Also note here and there fibrosis of the connective tissue, the whole revealing the presence of a hypoplastic kidney.

CASE 2.—*Nephrectomy for hypoplastic kidney.*

J. L., a man, aged 21, had been complaining of indefinite abdominal pain and urinary disturbances at different intervals for more than ten years. Three years ago he was admitted to the surgical ward of the New York Hospital where an appendectomy was done. Nine months later he had an operation for undescended right testicle. His chief complaint, when admitted to the urological department of the New York Hospital on Sept. 19, 1930, was pain on the left side of the abdomen and in the region of the left kidney; he also complained of intermittent pain in the right lumbar region accompanied by frequency of urination, dysuria, pyuria and urgency, and marked burning on urination. The pain was more marked in the left lower quadrant in the region of the lower left ureter. He had been treated elsewhere for cystitis and cystoscopy had been done on several occasions, but no definite diagnosis had ever been made. Cystoscopy was performed at the

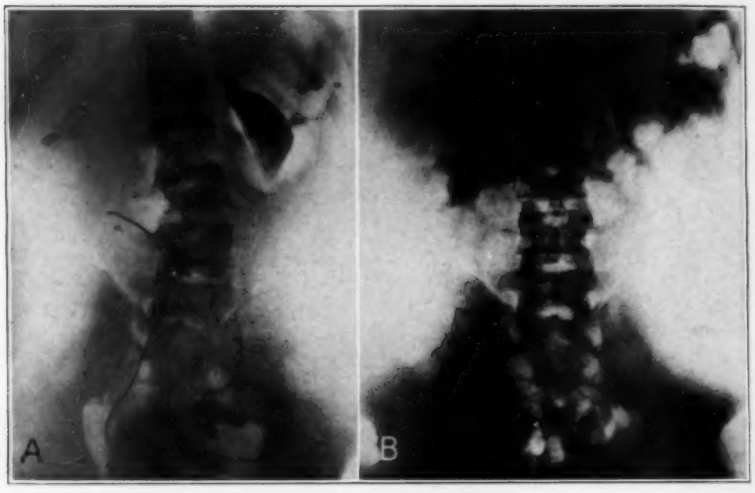


Fig. 5.— *A*, pyelo-ureterogram of the left side revealing an unusual shape of pelvis without calices and also a diverticulum of the lower portion of the ureter. *B*, pyelogram made in the same case after the injection of iopax, revealing good excretion of the opaque substance with presence of a slight hydronephrosis and good function of right kidney. Note the bizarre shape of pelvis on the opposite side, disclosing the presence of a congenital malformation of the left kidney, which was assumed to be a hypoplastic organ.

urological clinic of the New York Hospital on September 19; both ureters were catheterized, and a differential functional test made.

The specimen of urine from the right ureter was clear and contained 9 Gm. of urea per liter; that from the left ureter was also clear and contained 0.5 Gm. of urea per liter. The phenolsulphonphthalein test gave the following results: time of appearance from the right ureter, eight minutes; per cent of phenolsulphonphthalein, 3; time of collecting, ten minutes; from the left ureter, no phenolsulphonphthalein; time of collecting, ten minutes.

Microscopic examination of the sediment of the wet specimen from the right ureter showed 11 red blood cells and 18 epithelial cells per high power field; from

the left ureter, 18 white blood cells in clumps per high power field and many epithelial cells.

A roentgenogram and pyelogram of the left side showed a greatly distorted left kidney with complete absence of calices; also the ureterogram of the left side disclosed a diverticulum at the lower end and much distortion throughout. As there was practically no function on the left side, it was thought that the patient had either an atrophic or diminutive kidney on that side or possibly a tuberculous infection. Guinea-pig inoculation was done on several occasions, but no tuberculous infection was demonstrated. To check up these findings an intravenous injection of iopax was given, with the result that the right kidney was found to

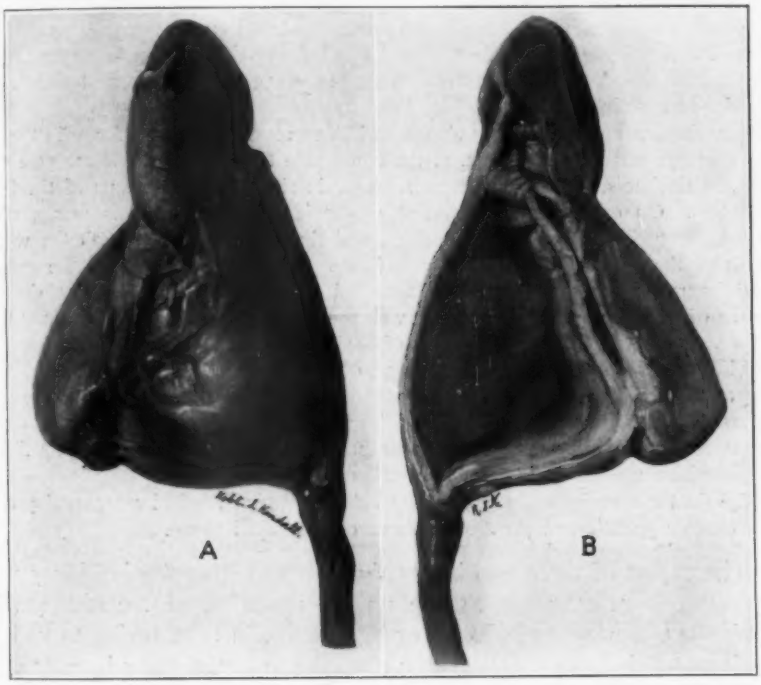


Fig. 6 (case 2).—*A*, drawing of the specimen removed at operation, showing evidence of an underdeveloped kidney with marked fetal lobulations and hydronephrotic plevis. *B*, sagittal view of the same, revealing that the renal parenchyma is here formed only of cortical substance and that there is no evidence of calices, papillae or medullary substance of the organ. This type of hypoplastic kidney, although having some excretory function, is incapable of undergoing compensatory hypertrophy and should be diagnosed by both the ascending and descending urographic methods.

have good excretion of the opaque substance, thus establishing the presence of a normal right kidney. In the left kidney, however, the elimination of the iopax did not appear for three hours, and the shadow thus obtained showed an irregular shape of the pelvis with absence of calices, thereby disclosing the presence of a pathologic or atrophic kidney, for which nephrectomy was recommended.

The operation was carried out on September 26. When the kidney was removed at operation, it was found to be infantile in type with a hydronephrotic pelvis and little cortex. When the organ was opened, it could readily be seen that it was formed only of cortical substance, that there were no pyramids, papillae or calices and that the thin and narrow margin of the cortical substance was attached to a hydronephrotic pelvis, as can be seen in the drawing here reproduced. The patient made an uneventful recovery, leaving the hospital eighteen days after the operation. But owing to the diverticulum left behind after an incomplete nephroureterectomy, he is at present complaining of some discomfort, for which he has been receiving cystoscopic treatments. He has been advised to have a secondary ureterectomy for the removal of the infected stump of the ureter and the diverticulum. The conclusion to be drawn from this case is that the presence of a congenital malformation of the kidney had been the underlying cause of the pathologic process, and that the organ was a hypoplastic kidney with practically no excretory renal function and, therefore, incapacitated to undergo compensatory hypertrophy in order to sustain life.

Examination of the specimen showed a kidney measuring about 9 cm. in length, with a width varying from 2 cm. at the upper pole to 6 cm. at the lower pole and 4 cm. in thickness. The organ was irregular in shape with remnants of the fetal lobulation. On opening the kidney, it was evident that the pelvis was greatly dilated, measuring about 3 cm. in width, and that it extended through the whole length of the kidney, like a thick-walled sac. Only the remnants of the calices could be seen; the pyramids were flattened out. Microscopic sections showed tubules which were on the whole quite well preserved. There was slight congestion of the vessels, including the capillaries of the glomeruli. A few of the tubules and capsular spaces contained a pink staining of homogeneous material. The epithelium of the pelvic mucosa was well preserved. The underlying fibrous tissue was increased in amount and contained a diffuse scattering of lymphocytes and a few plasma cells. The ureter showed some increase of fibrous tissue beneath its lining of epithelium, and also a diffuse infiltration of lymphocytes.

The final diagnosis was a hypoplastic kidney showing marked extrarenal pelvis, with chronic pyelitis and practical absence of pyramidal tissue.

The report of these two illustrative cases of hypoplastic kidney will serve to attract attention to this unique condition of the kidneys, in which the organ, when infantile or hypoplastic in type, owing to underdevelopment, is incapacitated for undergoing compensatory hypertrophy or for functioning efficiently enough to sustain life. It is essential that the surgeon be well acquainted with the clinical importance of this entity and be able to recognize it, in order to prevent fatal results. Today the diagnosis of this clinical condition is possible if based on the differential functional renal test and on the comparative study of pyelographic data, as the report of these two cases has demonstrated. It is very important, therefore, that the differential urographic diagnosis of the condition be borne in mind, since this abnormal type of kidney may readily be confused with the presence or the association of other different types of lesions, such as are frequently observed in the acquired or secondary atrophy of one kidney, due to tuberculosis, tumor, calculous diseases, pyelonephritis or hydronephrosis. These acquired types of pathologic process in the kidney are seen commonly at postmortem examination

and also on pathologic or clinical examination of cases. Furthermore, the hypoplastic kidney should always be differentiated from other common types of anomalies, such, for instance, as the double kidney, in which the appearance in the pyelogram of the upper pelvis alone, always

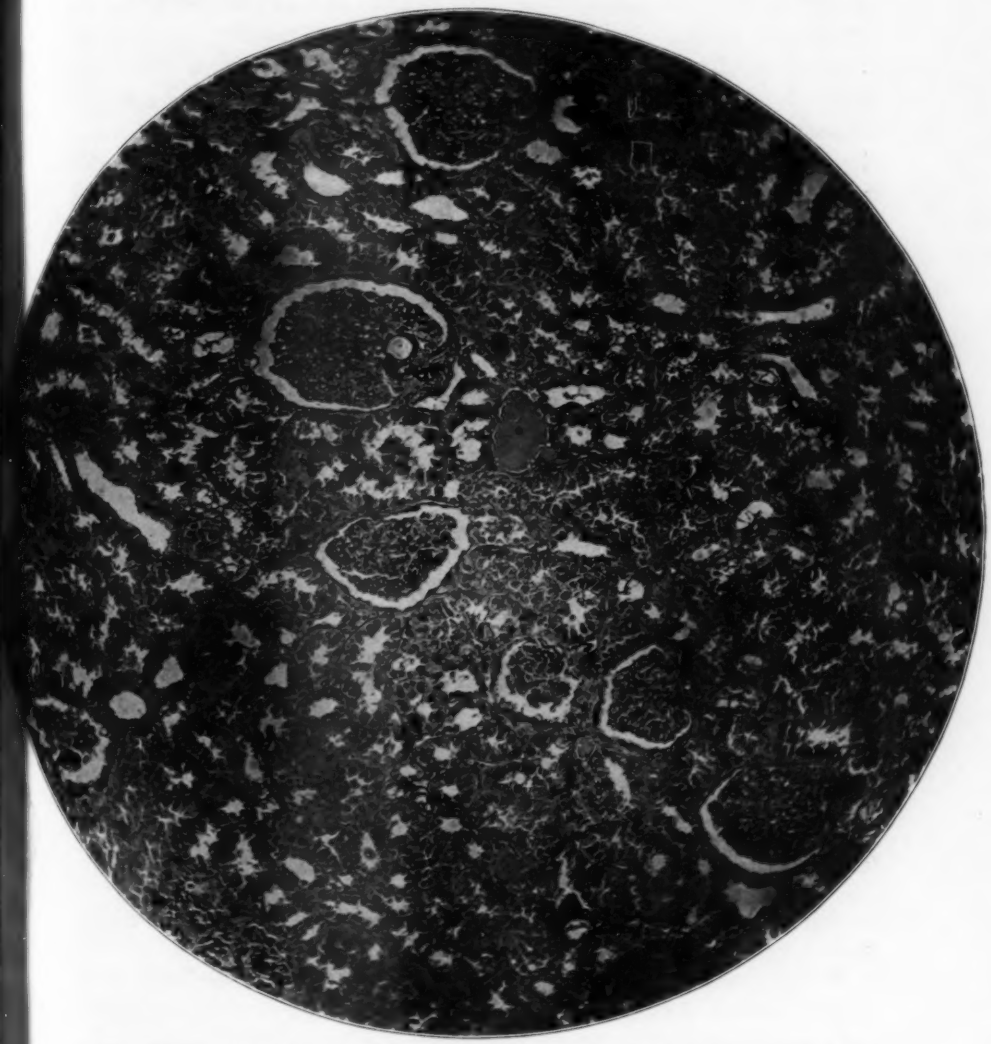


Fig. 7 (case 2).—Photomicrograph of section made from the removed specimen, in which the histologic studies reveal the presence of glomeruli and tubules of a normal kidney tissue, although the clinical appearance and the gross anatomopathologic data are obviously those of a hypoplastic kidney.

diminutive in size and assuming a T form or mushroom shape, causes a misleading interpretation of the urographic findings, if, in taking the

ureteropyelograms, the double pelvis and ureters have not both been properly visualized. This error is not infrequent when cystoscopy has been done by inexperienced hands, and is usually due to improper identification of the two ureteral orifices on the one side of the bladder or to failure to take the routine ureteropyelograms in cases in which the two ureters of the double kidney pelvis unite before reaching the bladder. A number of such cases have been seen in the clinic. Nowadays these could be easily checked up by the intravenous method of urography. Hence, these so-called rare anomalies of the upper urinary tract should be carefully looked for and identified by means of both urographic methods of taking urograms, since a diminutive or rudimentary pelvis

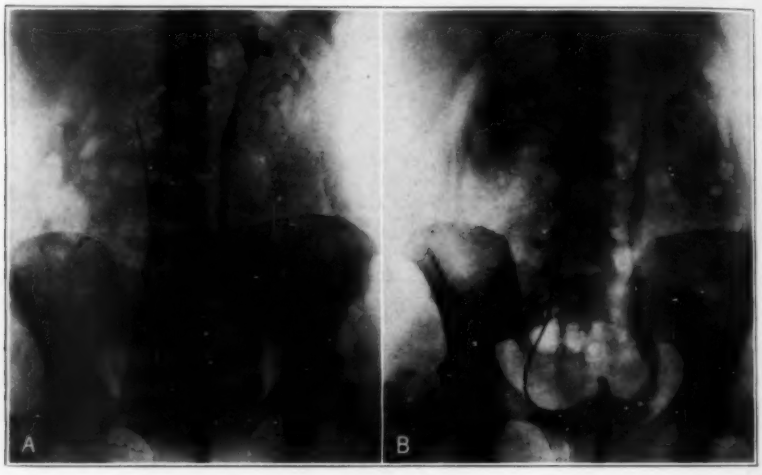


Fig. 8.—*A*, pyelo-ureterogram of the left kidney revealing a diminutive size of renal pelvis, resembling that of a hypoplastic kidney, when in reality such a T-shaped or mushroom-shaped pelvis indicates the presence of the upper pelvis of a double kidney. *B*, the two ureters of the same double kidney have been injected with the opaque substance and the pyelo-ureterogram shows the anomaly of a double kidney with double pelves and double ureters on the same side.

seen in a retrograde pyelogram is not always conclusive evidence of a hypoplastic kidney.

Finally, these three types of renal lesions under discussion have another generic relation or clinical similarity which it may be of interest to mention: namely, that the hypertrophic kidney, which is anatomically larger since physiologically it is carrying on the function of its mate, is commonly associated with nephritis and pyelonephritis, and consequently is always symptomatically painful. Both organs may, therefore, be affected at the same time with some other types of associated pathologic process. Hence, in this series of cases, it has been observed that the presence of persistent pain in both lumbar regions may mislead

at the outset in the clinical interpretation. Lumbar or abdominal pain on the one side is due to the pathologic position occupied by the hypertrophic and hyperfunctionating kidney, while on the other side it is usually caused by the hypoplastic or aplastic condition, in which, because of the lack of function and the chronic infection, the retained urine and the lack of dynamism cause renal nephralgia in the corresponding lumbar and abdominal regions. These clinicopathologic factors must, therefore, be borne in mind, since a hasty examination of a patient with a large palpable kidney on the one side might lead to a fatal operation, if the necessity for a differential renal functional test or pyelographic studies was not recognized.

Although a thorough examination and careful history are always important in the clinical study of any given case, the differential diagnosis in potential surgical anomalies or any other conditions of the kidney should always be based on the comparative estimation of the renal functional test and on the evidence obtained from the cystoscopic, roentgenographic and urographic data. In this way alone can a sound and permanent prognosis be assured.

RENAL APLASIA

The condition of unilateral renal aplasia may be best explained by saying that it is the extreme expression, in a clinical and anatomopathologic sense, of hypoplasia of the kidney, which is characterized by a congenital defect or arrest of development of one kidney, accompanied by hypertrophy of its mate. It is, however, differentiated from hypoplastic kidney in that the rudimentary and diminutive structure, supposed to be a renal organ, is a small mass of aberrant fibrous tissue, which, although it may be microscopically formed of embryonic and sclerotic or even calcified glomeruli and tubules, has at no time had any excretory function. Moreover, the excretory apparatus per se of pelvis, calices and ureter is absent or incompletely developed.

In the study of renal aplasia two types must be considered from a clinico-anatomopathologic standpoint.

First, there are those cases in which the fibrous mass of renal tissue, which may be found in the renal fossa or its vicinity, covered by the pararenal fatty capsule of the lumbar region, has a small or diminutive underdeveloped renal artery, which runs from the aorta to the aberrant amorphous mass of renal fibrotic tissue.

There is no evidence, however, of true renal pedicle, renal pelvis or patent ureter, although a short, rudimentary, incomplete and functionless ureter may always be discovered in the course of a careful postmortem examination. It is thus on the whole an organ which definitely has never shown any signs of existence in a true sense, or ever accomplished any anatomic or physiologic function. Nevertheless, because

of the presence of a diminutive renal artery, assuring a direct blood supply, it can eliminate into the mass of tissue the intravenously injected opaque substance, bringing out by the roentgenogram the surprising revelation of the presence of aberrant renal tissue and thus serving to establish a diagnosis.

The second group of cases of renal aplasia consists of those in which there is no evidence of a renal artery in the diminutive aberrant fibrous mass of connective tissue, and, therefore, no direct blood supply from the aorta or iliac arteries. All that exists is collateral branches coming from the suprarenals and surrounding tissues, so that no substance opaque to the roentgenograms can be eliminated to produce any shadow cast for diagnostic purposes. Furthermore, the pelvis and upper portion of the ureter are anatomically or histologically absent, but nevertheless there is always evidence of the remnant of a functionless and incomplete or obliterated ureter in the aplastic side of the urinary bladder.

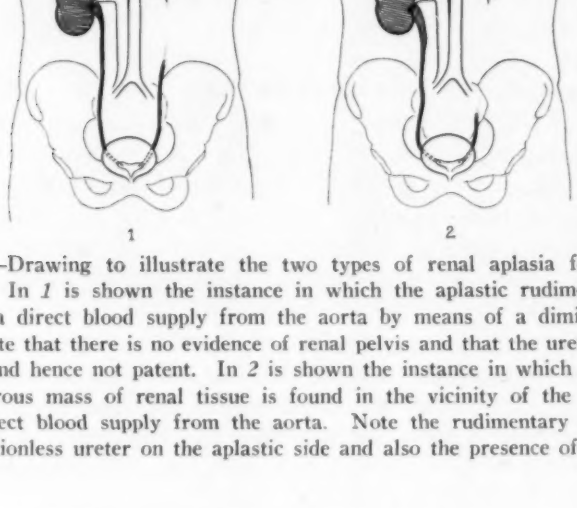


Fig. 9.—Drawing to illustrate the two types of renal aplasia found in the literature: In *1* is shown the instance in which the aplastic rudimentary renal organ has a direct blood supply from the aorta by means of a diminutive renal artery. Note that there is no evidence of renal pelvis and that the ureter is underdeveloped and hence not patent. In *2* is shown the instance in which an aberrant, aplastic fibrous mass of renal tissue is found in the vicinity of the renal fossa, without direct blood supply from the aorta. Note the rudimentary development of the functionless ureter on the aplastic side and also the presence of both suprarenals.

These two types of renal aplasia are the ones that I have been able to find in the misleading and confused literature of the report of cases, many of which have been recorded as congenital absence of one kidney when it is obvious that they were in reality instances of renal aplasia.

This rare condition of the undeveloped aplastic kidney has been observed occasionally at postmortem examination. Campbell [22] recently reported 39 cases from a series of 13,000 autopsies at Bellevue Hospital

22. Campbell, M. F.: Congenital Absence of One Kidney: Unilateral Renal Agenesis, Ann. Surg. **88**:1039, 1928; personal communication to the author.

and claims that renal aplasia is found four times more frequently than congenital absence of a kidney. This assertion is also confirmed by other authors, whose findings from postmortem examination and anatomopathologic studies have been reported in the literature (Schilling,[23] Risel,[24] Lorenz,[25] Pfeiffer,[26] Ballowitz,[27] Heilbronn,[28] Gruber and Bing,[29] Rosenbaum [30] and others). This condition has seldom, however, been discovered at operation, unless a previous cystoscopic and urographic investigation has revealed it, as in MacKenzie and Hawthorne's cases published in 1928.[31] But in reality, not until the present time, with the advent of pyelography following intravenous injection, has the accurate clinical diagnosis of renal aplasia ever been possible in the history of medical science.

The clinical and surgical aspect of this condition merits careful scrutiny, since the aplastic kidney has no eliminatory function. Surgical therapy must, therefore, continue to be along very conservative lines, particularly when a radical operation such as nephrectomy is contemplated.

Renal aplasia must, moreover, be differentiated from secondary or acquired renal atrophy, particularly in cases of occlusion or autonephrectomy due to disease or an associated pathologic process such as is commonly observed both clinically and at postmortem examination. The varieties of renal atrophy are readily seen in chronic inflammatory lesions of the kidney, in traumatisms, tuberculosis, hydronephrosis, pyonephrosis, nephro-ureterolithiasis and other acquired lesions in which the kidney may undergo complete destruction or atrophy.[32] These instances of associated pathologic process may be conceded to be the cause of the acquired or secondary type of renal atrophy, which does

23. Schilling, F.: Ein Fall von hochgradiger Aplasie der Nieren, Virchows Arch. f. path. Anat. **232**:176, 1921.

24. Risel, Hans: Ueber Nierenhypoplasie, Freiburg, Speyer & Kaerner, 1903.

25. Lorenz, F. H.: Hypoplasie und Aplasie der Niere, München, Kastner & Callwey, 1907.

26. Pfeiffer, E.: Die Nierenhypoplasie, Ztschr. f. urol. Chir. **16**:193, 1924; **23**:332, 1927.

27. Ballowitz, E.: Ueber angeborenen einseitigen vollkommenen Nierenmangel, Virchows Arch. f. path. Anat. **141**:309, 1895.

28. Heilbronn, Joseph: Ueber congenitale Nierenanomalien, Würzburg, Stahel, 1902.

29. Gruber, G. B., and Bing, Leo: Ueber Nierenmangel, Nierenkleinheit, Nierenvergrösserung und Nierenvermehrung, Ztschr. f. urol. Chir. **7**:259, 1921.

30. Rosenbaum, R.: Ueber doppelseitige Nierenaplasie, Frankfurt. Ztschr. f. Path. **41**:136, 1931.

31. MacKenzie, D. W., and Hawthorne, A. B.: Unilateral Renal Aplasia, Surg., Gynec. & Obst. **46**:42 (Jan.) 1928.

32. Gutierrez, R.: The Value of Indwelling Ureteral Catheters in Urinary Surgery, Surg., Gynec. & Obst. **50**:441 (Feb.) 1930; Indications and Technic of Combined Ureteronephrectomy, Ann. Surg. **93**:511 (Feb.) 1931.

not need to be emphasized at this time, because it is obviously well understood both clinically and by animal experimentation (Albarran,[33] Beer,[34] Hinman,[35] and Barney [36]).

In essential renal aplasia, which is an arrest in its development, the true kidney has never been formed. It has also been observed that there is no associated pathologic process or concomitant primary lesion except the sclerosis of the embryonic tissues, and that there is no sound explanation for the absence of the cortical, medullary and excretory renal parenchyma, other than the conception that it is the result of a lack of development during intra-uterine life, in which the mesonephros by an aplastic process has not formed or produced the definitive kidney. Hence it is to be assumed that the remnants of an aplastic renal tissue are due to the remains of the primitive nephrogenic tissue, which have been left behind through an arrest in its development. Furthermore, this assertion can be substantiated to a certain extent by the recent work of Bagg [37] on congenital defects in mice, in which there have been observed roentgenographically many instances of absence of a kidney and other malformations, such as the development of rudimentary and diminutive aplastic and hypoplastic kidneys.

Renal aplasia must also be differentiated from congenital absence of one kidney in which there is no anatomopathologic evidence of a diminutive organ or even vestigial, aberrant tissue, so that neither the hypoplastic nor the aplastic kidney is in existence. In order to get rid of the confusion that reigns in this field, in which many authors have reported cases of congenital absence of one kidney when in reality there was evidence of renal aplasia, or vice versa, it appeared to me that it would be useful to work out a clinicopathologic classification that would make possible the differential diagnosis between these three conditions. To this end, I have summarized the most important clinico-anatomopathologic points of distinction, in the classifications which can be seen in the introduction of this communication.

It is obvious that the fallacies of renal aplasia are the clue to errors in diagnosis, which sometimes lead to fatal consequences even when urologic examination has been carried out. Clinically, the patient has no symptoms related to the urinary tract, and merely complains of pain

33. Albarran, J.: Etude sur le rein des urinaires, Thèse Paris, 1889, no. 125.

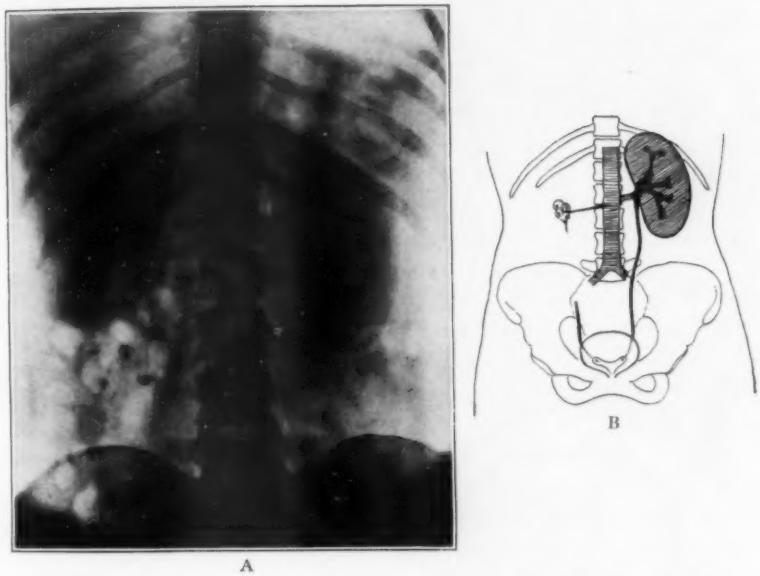
34. Beer, Edwin: Collected Papers, New York, Paul B. Hoeber, Inc., 1931, p. 234; Experimental Study of the Effects of Ureteral Obstruction on Kidney Function and Structure, Am. J. M. Sc. **143**:885 (June) 1912.

35. Hinman, F., and Morison, D. M.: Experimental Hydronephrosis, Surg., Gynec. & Obst. **42**:209 (Feb.) 1926.

36. Barney, J. D.: The Effects of Ureteral Ligation: Experimental and Clinical, Surg., Gynec. & Obst. **15**:290, 1912. Papin, E.: Les hydronéphroses, anatomie et pathogénie, avec un atlas, Paris, Doin et Cie, 1930.

37. Bagg: Am. J. Anat. **36**:275, 1925.

in the lumbar region; on cystoscopy the bladder appears, as a rule, to be normal, and there can be seen two normally placed ureteral orifices, although the ureter on the aplastic side is always obliterated and is therefore without excretory function. It can, however, be probed and admits a catheter no. 5 or no. 6 French for a distance of 4, 5 or 6 cm., but the remaining vesical portion of the aplastic ureter has never in any instance any physiologic function. The blind stump has no connection with the fatty mass of sclerotic renal tissue; consequently, since the pelvis of the kidney appears never to have been anatomically and physiologically formed, there is no excretion of urine. The ureter accordingly may be absent or partially absent, or may be found as a



A B

Fig. 10 (case 3).—Pyelogram in a case of renal aplasia following injection of iopax: *A*, the opaque substance has been eliminated with good concentration by the left kidney, revealing a normal pelvis and a hypertrophic left kidney. On the right side can be seen no outline of a kidney, but four faint shadows are cast by the roentgenogram, indicating that the opaque substance has been excreted by some renal substance, which served to establish a diagnosis of right renal aplasia. *B*, a drawing of the foregoing findings, which were confirmed at operation.

thin thread of fibrous tissue, closely adherent to the parietal layer of the lumbopelvic peritoneum and without clinical or pathologic significance. Furthermore, it can be observed clinically that when an opaque medium is injected into the catheterized aplastic ureter without excretory function, for the purpose of taking a pyelo-ureterogram, the ureter forces the fluid to regurgitate back into the bladder and does not allow it to go up the lumen. Thus no further investigation can be pursued, and only a hypothetic diagnosis is possible.

The blood supply is of extreme interest, since it may give the clue to the clinical or anatomopathologic diagnosis. At postmortem examination no kidney pedicle is ever found except a very elementary or rudimentary renal artery that may run from the aorta to this indefinitely fatty-renal, fibrous mass of tissue. Sometimes it is not possible to identify or find evidence of a true renal artery, and only the renal sclerotic mass of lipomatous tissue is observed, surrounded by innumerable aberrant blood vessels, which are collateral branches or anastomoses from the blood supply of the suprarenals. As a rule, there is no pelvis or ureter, but there may be found in the renal fossa, surrounded by a fatty capsule and bound down by fibrous bands of adhesions to the suprarenal, a small mass of fibrous tissue, formed by two or three small cysts attached together, representing dilatations of the renal tubules and apparently containing a few drops of yellow viscous fluid that may have the chemical characteristics of urine, as in MacKenzie's case and in the two cases that I am here reporting. This is why in taking a pyelogram following intravenous injection of any of the new drugs in use, a few tiny patches of shadow may be seen in the x-ray films, as in case 3 (fig. 10), in which the intravenous injection of iopax established the final diagnosis, which was suspected cystoscopically and confirmed at operation.

In the second case of renal aplasia here reported, the diagnosis was made at postmortem examination (see report of case 4) and the photograph of the specimen removed at autopsy plainly reveals all the characteristics of renal aplasia with its corresponding enlargement of the suprarenal gland (fig. 13).

The anatomopathologic characteristic in these cases of renal aplasia is that the histologic section of the specimen removed reveals, besides the anatomic features already described, the definite presence of renal tissue, characterized by embryonic or sclerotic tubules and glomeruli.

Sometimes the malpighian bodies may be occupied by deposits of lime or even calcification, and the elements of Bowman's capsule may undergo degeneration; there is also evidence of thick sclerosis of the blood vessels and connective tissue. The glomeruli have been invaded by connective tissue which appears to be undergoing hyaline degeneration. The matrix of this connective tissue is much degenerated and is formed of flattened epithelium; at some points there can be seen areas of calcification or complete sclerosis of the glomeruli, and sometimes dilatations and degenerations of the tubules to the extent of cyst formation, as in the instance of an underdeveloped polycystic kidney. Also, it is evident that the tubules may be found in groups and may appear very diminutive even under a high powered microscope. However, the problem of the histologic differentiation of renal aplasia from hypoplastic kidney and renal atrophy is almost incapable of solution by

microscopic studies alone, without taking into consideration the anatomo-clinicopathologic data already mentioned.

The symptomatology in renal aplasia, as in hypoplasia, is misleading, because these patients complain of pain in both sides of the abdomen. In the aplastic side this is due to the remnant of kidney tissue present; this acts as a foreign body, by virtue of the weight and irritant action of the amorphous renal mass, in which some of the glomeruli and tubules degenerate into cystic dilatations, which incarcerate a few drops

Fig. 11 (case 3).—Photomicrograph of a histologic section from a specimen removed at operation, revealing the presence of elements of renal tissue, and thus confirming the presence of an aplastic renal organ. Note that the histologic studies disclose the presence of rudimentary and also of dilated tubules with marked sclerosis of connective tissue, thickening of the blood vessels and calcification of the glomeruli.

of urine and ultimately, for lack of drainage, tend to form calcifications, and also to produce pressure on the surrounding tissues, thereby causing reflex symptoms and indefinite abdominal pain. In the other side, the pain is caused by the excessive size of its mate, which is anatomically and physiologically enlarged and overworked, resulting in compensatory

functional hypertrophy and, therefore, leading to painful symptoms here also. This bilaterality of symptoms must always be borne in mind in establishing the diagnosis.

The treatment of renal aplasia, whenever it is diagnosed, is surgical. It consists of the removal of the remnants of the aplastic functionless kidney with as much as possible of the pararenal fatty capsule.

The two illustrative cases of renal aplasia that I am reporting for the purpose of placing them on record are as follows:

CASE 3.—*Exploratory lumbo-abdominal operation in case of renal aplasia diagnosed previous to the operation.*

M. S., a housewife, aged 32, was admitted to the second surgical division of the New York Hospital, Nov. 2, 1931, and the case is here reported by courtesy of the director of the service, Dr. E. H. Pool, and the attending surgeon, Dr. S. Erdman. The chief complaint was pain in the right lumbar quadrant of over two years' duration. The patient had been examined elsewhere, and her condition was diagnosed as colitis, cholelithiasis, stone in the kidney or chronic appendicitis. She had slight frequency and nocturia but never recalled having had hematuria or pyuria. There was no history of trauma or of any operation performed previous to admission.

On physical examination, she was seen to be a rather obese widow of 32, looking in no way acutely or chronically ill. The kidneys were not palpable, and no mass or abdominal distention was made out. There was no tenderness, but just to the left of the umbilicus a dull pain was present, radiating toward the right lumbar region.

After the routine general laboratory and roentgen examinations of the gallbladder and gastro-intestinal tract, the patient was sent to the urological department for examination. On cystoscopy, the interior of the bladder was found to be normal except for a slight congestion around the right ureteral orifice. The left ureteral orifice was normal in size, shape and position. Both ureters were catheterized. A no. 6 French catheter met an obstruction in the right ureter about 5 cm. from the bladder. On the left side, the catheter was passed to the pelvis of the left kidney without obstruction. A specimen was collected from the left kidney for culture, urea and microscopic examination, but no specimen could be collected from the right side. One cubic centimeter of phenolsulphonphthalein was injected intravenously and appeared in three minutes from the left side. No specimen or color dye could be obtained from the right ureter. X-ray pictures and a pyelogram were taken. The roentgenogram revealed no shadow indicative of stone anywhere in the urinary tract, but the outline of the left kidney was enlarged and could be definitely made out, while on the right side no renal shadow or outline of the kidney could be seen, and the sodium iodide injected into the right ureter regurgitated back into the bladder. Hence no pyelogram could be obtained on the right side. In view of this finding, a pyelogram after intravenous injection of iopax was advised. After various plates were taken, the outline of the pelvis of the left kidney was clearly made out; the plate revealed good excretory function with the presence of a normal pelvis, and apparently an enlarged hypertrophic kidney. In contrast to this, on the right side, no outline of any kidney could be seen, but four tiny indefinite shadows, each about the size of a pea, appeared at the level of the third and fourth lumbar vertebrae in the region of the renal area, giving a definite impression that the iopax had been excreted by some kidney substance. No definite evidence of pelvis or kidney could be made out. However, in view of the unusual

shadow brought out by the intravenous injection of iopax, associated with complete absence of renal function and impatency of the same corresponding right ureter, it was concluded that the patient should be submitted to an exploratory operation. It was assumed that a pathologic condition of the right kidney, possibly of congenital origin as in renal aplasia, was being dealt with. At operation a right lumbar oblique incision was made, and the fatty capsule opened, but no kidney was found. Instead, the operation revealed a small irregular, fatty, fibrous mass, which was clamped, tied and removed. The small shapeless mass of fibrous renal tissue was surrounded by blood vessels and bound down by adhesions, but no evidence of pelvis or ureter was identified or made out. The peritoneum was deliberately opened through the same lumbar incision, in order to explore the abdominal cavity, and on palpation the gallbladder and appendix were found to be normal. Moreover, an extensive exploration into the right lumbar region and down to the iliac fossa failed to reveal the presence of anything resembling a kidney. The posterior side of the peritoneum was also examined, for evidence of a possible ureter, but none could be traced or identified. Accordingly, the peritoneum was closed by a continuous suture and the exploratory operation was finished in the usual manner, closing the wound in layers without drainage. An uneventful convalescence followed, and the patient was discharged twelve days later in an improved condition. The pathologic report of the specimen removed at operation showed the presence of distorted, aberrant, renal tissue with sclerosis of the blood vessels, cyst formation and areas of calcification, as can be seen in the photomicrograph (fig. 11).

This case is perhaps the first to be put on record in which the diagnosis of renal aplasia was made urographically by the excretion of iopax administered intravenously. It may be concluded that in future cases of renal aplasia or other congenital malformations of the kidney, when accompanied by a small or rudimentary renal artery, pyelograms made following intravenous injection of iopax will serve to confirm and clarify the diagnosis, which in this case was hypothetically made by cystoscopy and retrograde pyelography.

CASE 4.—*Nephrectomy for multiple cortical abscess in a case of unilateral renal aplasia.*

Mrs. M. K., aged 30, a housewife, was admitted to the surgical ward of the New York Hospital on Dec. 16, 1915, and the case is here reported by courtesy of the director of that service, Dr. Eugene H. Pool. The chief complaint was pain in the right lower quadrant with vomiting and nausea. The patient had been acutely ill for two days previous to admission. Except for a persistent dull pain in the right lower quadrant during the last year, the past history was irrelevant.

On physical examination, the abdomen was rather large and rigid, making the palpation of deep organs almost impossible. Urinalysis showed a heavy, cloudy urine, and the eighteen hour specimen was 390 cc.; specific gravity, 1.013; reaction, acid; color, amber with presence of albumin and many epithelial cells; red and white blood cells were also present. In view of this finding, an x-ray picture was taken to rule out the possibility of urinary calculi. Cystoscopy was advised, but was not done, because the patient was menstruating, and moreover, her critical condition did not warrant delay. In view of the tenderness on the right flank, the palpable mass in the region of the appendix, the acute symptoms and the negative x-ray findings, the surgeon thought it advisable to explore the region of the appendix and gallbladder. Accordingly, on December 17, under general anesthesia, a

short right rectus incision was made, which established that the appendix and gallbladder were normal and that the mass was positively a kidney condition. The midline incision was then closed by layers, and the patient turned over into position for kidney operation. An oblique lumbar incision was made to expose the kidney, which was found to be large and to be surrounded by inflammatory adhesions of the perirenal fat and other structures. The surgeon's idea was only to drain the abscess of the kidney, on account of the extremely grave condition of the patient, since, as cystoscopy had not been performed, it was, of course, not known whether or not there was another functionating kidney on the other side. A nephrotomy was accordingly done in order to drain the multiple cortical abscess, but so much hemorrhage resulted that it became necessary to clamp the pedicle and perform a rapid nephrectomy in order to stop the profuse bleeding. The wound was closed, and the patient returned to the ward in poor condition. Five days later, as she was not eliminating any urine and was in a grave uremic condition, another operation was performed on the opposite side under general anesthesia in order to explore the condition of the left kidney. To the surgeon's surprise no left kidney

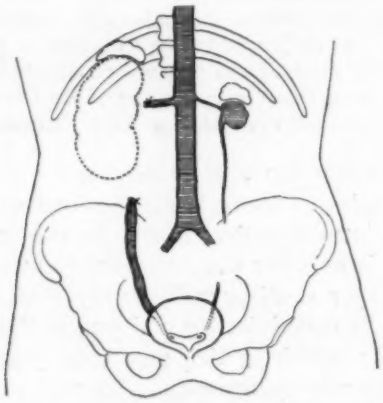


Fig. 12 (case 4).—Drawing in which right nephrectomy was done for multiple cortical abscess of the right kidney in presence of left renal aplasia discovered at postmortem examination. (No pyelogram of this case is available, since it occurred before the establishment of the urologic department.)

was found in the left lumbar region after a full exploration of the intraperitoneal and extraperitoneal cavity. The wound was closed without drainage after the congenital absence of the left kidney was ascertained. The patient suffered with complete suppression of urine and died in uremic coma four days after the second operation. The postmortem examination of this case, performed on December 26, revealed that the right kidney had been removed at operation and that the right renal artery was occluded by a thrombus following ligation of the vessel. In the area of the left kidney a structure was found which represented the remains of an imperfectly developed kidney. This structure gave the impression that the left kidney was present only in a rudimentary stage. Its surface was covered with a fibrous capsule, showing numerous small blood vessels radiating toward the hilus of the organ. A section of the structure revealed the presence of a markedly underdeveloped organ, in which the pyramidal and cortical substance could not be differentiated. The left rudimentary renal artery led to a flat crescent-shaped mass of tissue situated below the left suprarenal, and measuring 3 by 0.8 by 0.6 cm.

(fig. 13). The hilus was occupied by a cystlike structure which represented the pelvis. It was about the size of a bean and was filled with a clear, amber-colored fluid. The interior of this cavity communicated directly with a small, rudimentary ureter, which permitted the passage of a small probe, measuring 2 mm. in diameter. The lumen of this ureter was partially patent, and was found to be rudimentary. It was like a thin cord adhering to the peritoneum, and consisted of a separate upper and lower part without any connecting passage. A photograph of the specimen removed at postmortem examination showed an aplastic renal artery and a ragged mass of aberrant renal substance. A small portion of the

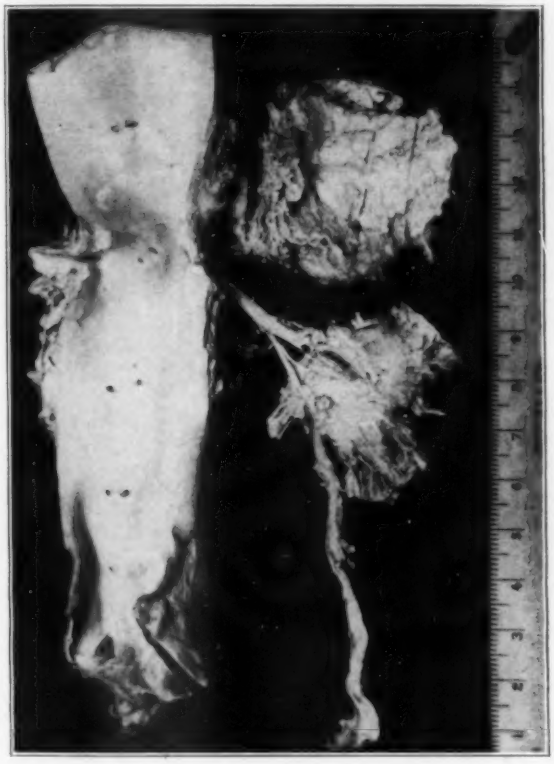


Fig. 13 (case 4).—Photograph of specimen removed post mortem showing the abdominal aorta, an enlarged left suprarenal gland and a mass of aberrant renal tissue representing an aplastic kidney, in which can be seen a rudimentary renal artery, coming from the aorta, and also a rudimentary functionless ureter (see case report).

ureter was constricted, but apparently without the formation of a renal pelvis or calices. On each side of the aorta, however, a thick and enlarged suprarenal was present.

The histologic section of this mass of tissue revealed the presence of embryonic glomeruli and tubules, thereby implying that it was a case of renal aplasia.

This case is a startling lesson and is very instructive in that it brings out the importance of preliminary cystoscopy and complete

urologic and urographic examinations in acute or chronic abdominal conditions, where the diagnosis is in doubt—particularly in cases in which urinary symptoms are present—and in which the routine urinalysis shows microscopic pyuria or hematuria. However, back in the days when this patient was operated on, the urologic department in the hospital had not been established, and not every patient was put through the routine urologic examination as today. Account must also be taken of the fact that the patient came to the hospital with acute abdominal

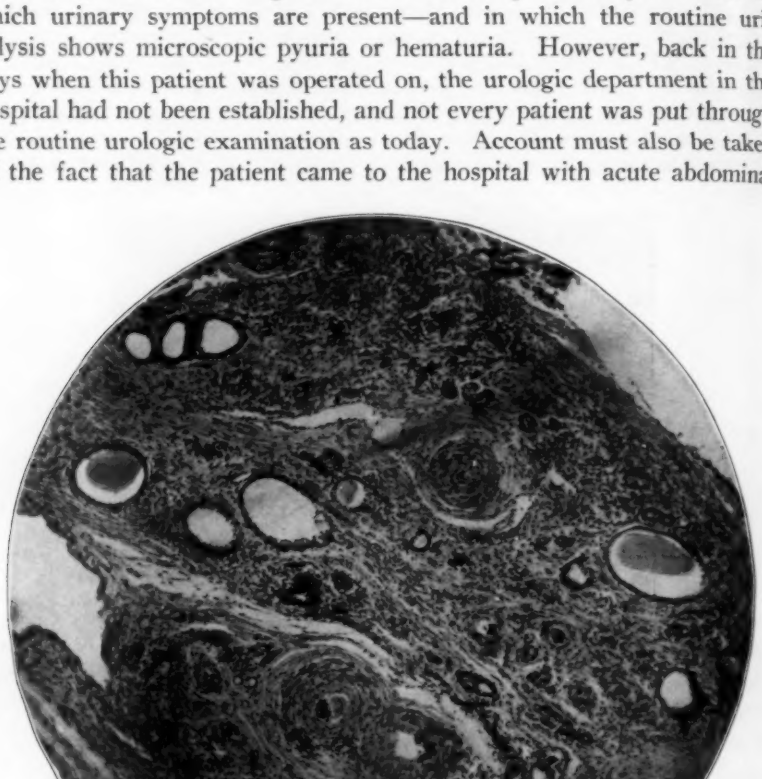


Fig. 14 (case 4).—Photomicrograph of section made from specimen removed post mortem from the left aplastic kidney, revealing the presence of embryonic renal tubules with degeneration and marked hyalinization of the glomeruli, also thickening of the blood vessels and connective tissue. There is a marked tendency to cyst formation of the tubules and the glomeruli.

symptoms, not regarded as kidney disease. The coincidence that cystoscopy is seldom done in the case of a patient menstruating must also be borne in mind. There was, moreover, for immediate consideration the acute condition of the patient, which required surgical intervention without further delay and which unfortunately had a fatal outcome. From this case, as from many others reported in the litera-

ture, the lesson to be learned is that, in operations on the kidney, the surgeon must always bear in mind the possibility of a congenital malformation—lack of function in the opposite kidney, absence or lack of development in one of the kidneys, or the many other varieties of surgical anomalies, which are commonly found in this urographic era of accuracy in diagnosis. This case is obviously a graphic example of renal aplasia with a concomitant pathologic process in its opposite hypertrophic mate, in which type of case only conservative surgical measures and urologic treatment are properly indicated.

CONGENITAL ABSENCE OF ONE KIDNEY

Congenital absence of one kidney signifies the complete lack of development of one of the twin organs, and represents a picture in which neither the hypoplastic nor the aplastic condition is present.

The absence of one kidney has been described in the literature from the time of Aristotle.[38] Valsalva,[38] Cruveilhier,[3] Morgagni,[2] Rayer[6] and other writers of a past age have all mentioned this rare anatomic anomaly found at postmortem examination. It has also been found occasionally during an exploratory abdominal operation, but the clinical diagnosis, in advance of operation, was never possible until cystoscopy and urography came into use.

Practically all the cases recorded in the literature up to the urographic era were discovered at postmortem examination. In 1863, Mosler[39] was among the first to make a collection of cases, reporting 14 that he found in the literature. Then Beumer,[40] in 1878, collected 44 such cases. But it was Ballowitz[27] who in 1895, did the important work of collecting and tabulating from the literature the descriptions of 213 cases, many of which were not actually instances of total agenesis of one kidney. Many other cases have meanwhile been reported and the literature has been reviewed on several occasions: by Moore[41] in 1898, by Radasch[42] in 1908, by Anders[43] in 1910, by Dorland[44] in

38. Quoted by Rayer: Traité des maladies des reins, Paris, J. B. Baillière, 1841. Morris, quoted by Henry: Surgical Diseases of the Kidney and Ureter, Including Injuries, Malformations and Misplacements, London, Cassell & Co., 1901, vol. 1, p. 18.

39. Mosler: Arch. d. Heilk. **10**:289, 1863.

40. Beumer: Ueber Nierendefecte, Virchows Arch. f. path. Anat. **2**:344, 1878.

41. Moore, F. C.: Unilateral Renal Aplasia, J. Anat. & Physiol. **33**:400, 1898-1899.

42. Radasch, H. E.: Congenital Unilateral Absence of the Urogenital System and Its Relation to the Development of the Wolffian and Müllerian Ducts, Am. J. M. Sc. **136**:111 (July) 1908.

43. Anders, J. M.: Congenital Single Kidney with the Report of a Case: The Practical Significance of the Condition with Statistics, Am. J. M. Sc. **39**:313 (March) 1910.

44. Dorland, W. A. N.: A Consideration of Renal Anomalies, Surg., Gynec. & Obst. **13**:303, 1911.

1911, by Eisendrath [45] in 1923 and by Goldstein [46] in 1925. More recently, Collins [47] of the Mayo Clinic summarized the study of 581 cases of congenital unilateral renal agenesis, among which he has included 9 from the Mayo Clinic, from a series of 6,349 consecutive postmortem examinations, thus representing an incidence of 1 in 705 cases.

It appears, however, that most of the writers who have discussed the abnormality of the absence of a kidney have failed to differentiate this condition from the fused kidney, the aplastic kidney, the hypoplastic kidney and the atrophic kidney, as I have already pointed out. Many authors who have reported cases of unilateral renal agenesis have described the presence of an aberrant aplastic or hypoplastic mass of renal substance, or of connective tissue, or of a rudimentary and incomplete ureter on the opposite side, representing an incomplete development of nephrogenic tissue, which obviously cannot be accepted as the essential and genuine absence of one organ in an anatomic or histologic sense.

TABLE 1.—*Cases of Congenital Absence of One Kidney as Collected from the Literature on the Basis of Postmortem Findings*

	Number of Cases	Left Kidney Absent	Right Kidney Absent	Side Not Indicated	Female		Male	
					Left	Right	Left	Right
Ballowitz	213	117	88	8	70	42	31	34
Mankiewicz	236	127	97	12	76	47	31	34
Cadoré	278	136	96	46	78	44	31	32
Cathelin	22	10	10	2	1	1	8	7
Campbell	10	6	4	..	2	2	4	1
Braasch	9	8	1	..	4		5	
Collins, D. C.	581	318	238	25	231		281	

Accordingly, from a close scrutiny of the literature with reference to the tabulation and description of all the cases reported, and also from my own observation, I have come to the conclusion that approximately from 35 to 40 per cent are not in reality authentic cases of unilateral renal agenesis, and that this is the reason why some other writers have gone so far as to state that renal aplasia is four time more common than congenital absence of one kidney. Finally, in order to differentiate these three conditions under discussion, I have made a classification based on the clinico-anatomopathologic data which can be seen in the tabulation in the introductory section.

In this section, therefore, I shall deal only with the cases of complete unilateral renal agenesis or congenital absence of one kidney, most commonly described as unilateral solitary kidney. But in the surgical study

45. Eisendrath, D. N.: Congenital Solitary Kidney, Ann. Surg. **79**:206, 1924.

46. Goldstein, A. E.: Congenital Absence of One Kidney: Review of Literature and Report of Two Cases, South. M. J. **18**:750 (Oct.) 1925.

47. Collins, D. C.: Congenital Unilateral Renal Agenesis, Proc. Staff Meet., Mayo Clin. **6**:581 (Sept. 30) 1931.

of congenital absence of one kidney, the cases fall into two groups when regarded from a clinico-anatomopathologic point of view. The first group contains the type of the true solitary single kidney in which there is complete absence of both the kidney and ureter on the one side. The single renal organ may be found in ectopic or cross ectopic position, but in this type of total agenesis there is only one ureteral orifice opening into the bladder and half of the trigone has not been developed. As a rule, this anomaly is accompanied by some form of congenital malformation, particularly of the genital tract, as can be seen in two of the cases that I am here reporting (cases 5 and 6).

The second group consists of the type of the solitary fused kidney, in which there is evidence of union of two nephroblastemas into one

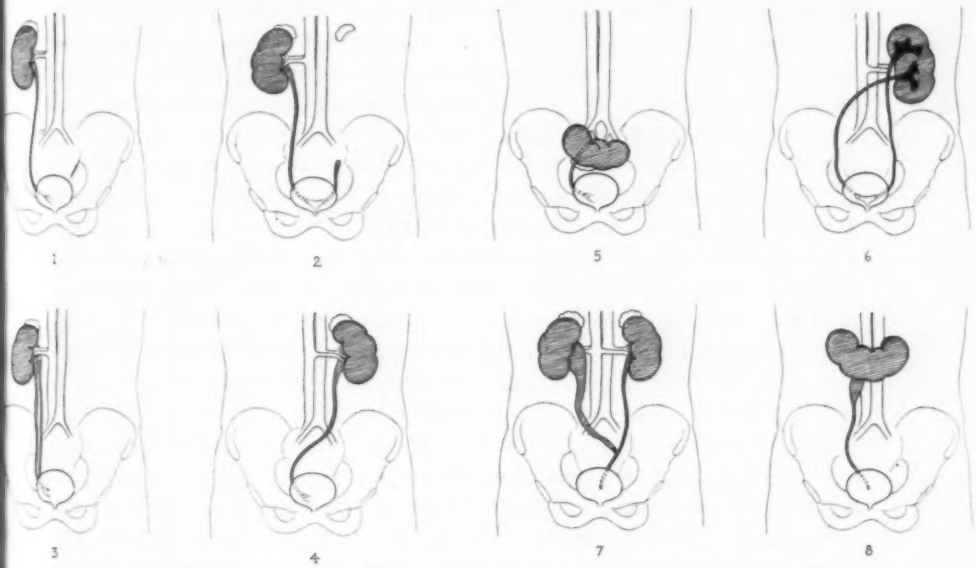


Fig. 15.—Drawing of the different types of congenital absence of one kidney, as collected from the literature: *1*, the true congenital solitary single kidney, in which half of the trigone is absent, and there is only one ureteral orifice opening into the bladder (note the absence of the renal artery on the opposite side and also of the corresponding suprarenal capsule); *2*, instance erroneously recorded as solitary kidney, when there is anatomic evidence of nephrogenic tissue on the other side; *3*, solitary fused single kidney with two ureters opening independently into one side of the bladder; *4*, solitary single kidney with ureter in cross ectopia; *5*, solitary ectopic single kidney; *6*, fused solitary kidney with two pelves and two ureters in cross ectopia, opening normally into the bladder; *7*, the rare instance of a single ureter formed by the fusion of the ureters from two separate kidneys; *8*, horseshoe kidney with a single pelvis and ureter and absence of trigone. Note that the essential congenital solitary single kidney is represented in drawings *1*, *4* and *5*, and that with the exception of *2* and *7*, the others are varieties of fused kidney.

organ, characterized by the presence of two pelves and two corresponding ureters, which may open either normally or abnormally into the bladder (fig. 15, nos. *3* and *6*). Of this variety of fused kidney, which is so frequently confused in the literature with congenital absence of one kidney, I am reporting an interesting example in case 8 of this series. Elsewhere, I have described [48] the different types of renal fusion, classifying them according as they present a symmetrical or an asymmetrical form of renal union. The symmetrical form is the typical horseshoe kidney, while the asymmetrical embraces such forms of unilateral renal fusion as the L-shaped mass, the sigmoid, the hour-glass, the ring-shaped or the fusion in cross ectopia. All of these are characterized by the presence of two corresponding pelves and two ureters, and hence should not be confused with the true solitary kidney, i. e., the congenital absence of one kidney. Furthermore, in the collection of unusual cases recorded in the literature and portrayed in the drawings of solitary kidney in figure 15, I have inserted the rare condition of a single ureter with two kidneys, an anomaly that has been recorded in the literature only three times, by Hepburn,[49] von Hansemann [50] and Braasch,[51] who made the diagnosis in vivo by pyelography. This condition, no doubt, is misleading in the diagnosis because there is only one ureteral orifice opening into the bladder and because clinically or cystoscopically there appears to be a single solitary kidney, when in reality it is a single ureter with two separate kidneys. Obviously, this rare anomaly can be discovered by the intravenous urographic method or by the routine method of taking ascending and descending pyeloureterograms.

Embryologically, the complete absence of one kidney is best explained hypothetically as a developmental defect of organic origin, in which the nephrogenic membrane or elements of the wolffian duct undergo an arrest in their development of the primitive nucleus, which never has been formed on the one side; hence the corresponding half of the urinary apparatus is absent from the earliest period of intra-uterine embryonic life. It is also of interest to note in this connection the marked frequency with which genital anomalies are met in these cases of unilateral renal agenesis. The corresponding müllerian duct on the agenetic side is also absent, and this embryonic defect is directly responsible for the absence of the genital organs, obviously more strikingly observed in the female than in the male, because the genital organs

48. Gutierrez, R.: The Clinical Management of the Horseshoe Kidney, Am. J. Surg. **14**:657 (Dec.) 1931; **15**:32 (Jan.); 345 (Feb.) 1932.

49. Hepburn, quoted by Eisendrath.[45]

50. von Hansemann, quoted by Papin: Chirurgie du rein, Paris, Doin & Cie, 1928, vol. 1.

51. Braasch, W. F.: The Clinical Diagnosis of Congenital Anomaly in the Kidney and Ureter, Ann. Surg. **56**:726 (Nov.) 1912.

of the female are derived from the müllerian duct. It should, therefore, be assumed that the absence of vagina and uterus or any other important anomaly of the genital tract in the female suggests the enormous probability, amounting almost to a rule, that there is also congenital absence of one kidney. The incidence and multiplicity of these varieties of anomalies of the genital tract have been well discussed in the literature, and according to the statistics on record they are met with in approximately 70 per cent of cases where one kidney is absent.

Since the Ballowitz report appeared in 1895, the association of genital and renal anomalies has been further emphasized by Guizzetti and Pariset,[52] Winter,[53] Bolaffio,[54] Engel,[55] Eismayer,[56] Papin,[57] Eisendrath,[45] and more recently by Collins.[47] The last-named author has recorded the presence of 338 genital anomalies in 581 cases of congenital solitary kidney, 129 being in males and 209 in females.

It is obvious that, with the multiplicity of embryonic malformations of both the genital and the urinary system, one may reasonably expect that the complete absence of the nephroblastema elements will rather frequently involve some other anatomic structures. When the kidney is absent, it is clear that the blood supply on that side is also absent, and the aorta at autopsy shows, in fact, no evidence or vestige of any branch of a possible renal artery on the agenetic side of the body.

It is significant from an embryologic and histologic point of view that the suprarenal gland is developed from two different sources which combine to form the complete organ. It is known that the cortical and the medullary portions of the suprarenal are formed from two different tissues. The cortical portion is derived from the columns of cells which bud off from the wolffian body, and is therefore of mesoblastic origin. The medullary portion of the gland, on the other hand, is developed in connection with the sympathetic nervous system and so is mainly of epiblastic origin. Hence, as the nephrogenic tissues of the wolffian duct are absent and have not developed the definitive kidney, it is assumed that the suprarenal, lacking one of its essential elements, is also absent.

This embryo-anatomohistologic conception of the derivation and formation of the suprarenal gland offers a basis for a new theory, that when a kidney is not formed the suprarenal gland on the corresponding agenetic side is likewise not formed. This theory may serve to estab-

52. Guizzetti and Pariset: Beziehungen zwischen Missbildungen der Nieren und der Geschlechtsorgane, Virchows Arch. f. path. Anat. **204**:372, 1911.

53. Winter: Arch. f. klin. Chir. **69**:611, 1903.

54. Balaffio: Ztschr. f. Geburtsh. u. Gynäk. **68**:261, 1911.

55. Engel, D.: Beitr. z. path. Anat. u. z. allg. Path. **67**:549, 1920.

56. Eismayer, G.: Malformations of the Uterus and Kidney, Ztschr. f. urol. Chir. **11**:191 (Jan.) 1923.

57. Papin, E.: Chirurgie du rein, Paris, Doin et Cie, 1928, vol. 1, p. 137.

lish a new index of great importance for the differentiation of renal agenesis from renal aplasia or hypoplastic kidney, as in the last two instances the suprarenal is invariably present. This assertion can be further substantiated by the report from the Mayo Clinic in which Collins [47] stated that in 581 cases of congenital unilateral renal agenesis, the condition of the suprarenal gland was as follows: absent on one side in 66; atrophic in 4; normal in 129; hypertrophied in 13, and *not stated in 369* (italics mine), which if added to the 66 in which authors stated there was absence brings a clearcut total of 429 cases in which there is no evidence that a suprarenal was ever present.

The recent report by Campbell [22] of 10 cases from 13,000 autopsies at Bellevue Hospital also shows that the suprarenal was in every case either absent or not recorded, as can be seen in his table (table 2).

Moreover, Collins,[47] in tabulating the cases that he has studied, described the condition of the ureters in the 581 cases as follows: Both ureters were present 99 times and both were completely patent 8 times; both ureteral orifices into the bladder were patent 25 times, and the ureter on the side of the absent kidney opened into the seminal vesicle 16 times, making a total of 148 instances in which the unilateral renal agenesis obviously was not complete. These, therefore, were cases of renal aplasia or hypoplastic kidney, and in these conditions the suprarenal, as I have already pointed out, is always present, whereas, on the contrary, the suprarenal is always absent in cases of unilateral renal agenesis or of congenital absence of one kidney.

The human kidney is so vital to life and is so commonly affected by disease that in an ordinary clinical or urologic investigation the first consideration is always to make certain of the presence of two organs. Hence, it is of paramount importance to the surgeon and urologist that he assure himself of the presence of a well functionating kidney, particularly when a surgical procedure for disease or associated pathologic process in its mate is contemplated.

In view of the various problems involved, the unexpected finding of a solitary kidney, predisposing to disease or carrying a fatal prognosis, has awakened the interest not only of the pathologist and embryologist but, to an even greater extent, that of the surgeon and urologist, since by the use of modern urologic methods of cystoscopy, the renal functional test, pyelography and roentgenography, with their superlative accuracy, the diagnosis can now be readily established without the necessity of waiting for an autopsy.

In the surgical aspect of congenital absence of a kidney, the danger of the condition lies in the fact that regardless of the anatomic position that the kidney may occupy the single organ is nearly always potentially affected with some chronic disease, such as nephritis, interstitial nephritis, pyelonephritis or other types of associated pathologic process,

TABLE 2.—*Cases of Congenital Absence of One Kidney Showing the Common Coincidence of Congenital Defects Observed at Postmortem Examinations in a Series of Nine Cases at Bellevue Hospital*

Case	Age	Sex	Side	Suprarenal	Renal Vessels	Ureter	Bladder	Genitalia	Principal Disease	Remaining Kidney
1. M. S.	1 mo.	F	L	Absent	Absent	Absent	No dimple	Unicorn uterus; no left fallopian tube; atrophic ovary	Marasmus	Normal
2. R. T.	5 da.	F	L	Not recorded	Absent	Absent	No orifice	Unicorn uterus; suprapelvic left ovary; perineal maldevelopment	Pneumonia	Normal
3. A. C.	36 yr.	F	R	Absent	Absent	Fibrous thread	No orifice	Grossly normal	Carcinoma of breast	Ureter and kidney dilated without obstruction; kidney large and flabby
4. S. Y.	36 yr.	M	R	Absent	Absent	Absent	No dimple	Right testicle atrophic, retroperitoneal; right seminal vesicle and vas deferens atrophic	Pneumonia	Normal
5. K. M.	35 yr.	M	L	Absent	Absent	Absent	No orifice	Grossly normal	Uremia	Scarred kidney of nephritis
6. J. F.	40 yr.	M	L	Not recorded	Absent	Absent	No orifice	Grossly normal	Pulmonary tuberculosis	Hyperplastic
7. C. J.	69 yr.	M	L	Not recorded	Absent	Absent	Dimple	Grossly normal	Pneumonia	Hyperplastic
8. M. M.	54 yr.	F	R	Not recorded	Absent	Absent	Dimple	Grossly normal	Endocarditis	Multiple infarction; left kidney much enlarged
9. S. M.	1 yr.	M	L	Not recorded	Absent	Absent	No dimple	Grossly normal	Uremia	Acute focal suppurative nephritis

predisposing to urinary stasis, owing to lack of drainage plus infection, hydronephrosis or stone formation, most commonly terminating in anuria, fatal uremia and death. The literature, in fact, abounds in reports of cases of anuria and death due to a solitary single kidney, and the report from the Mayo Clinic,[47] is very convincing when the condition of the remaining kidney is described as normal in 281, diseased in 179 and not stated in 121. There were 110 subjects who died from disease of the genito-urinary tract, namely, pyelonephritis, 27 cases; nephrolithiasis, 24; ureterolithiasis, 16; chronic nephritis, 13; hydronephrosis, 12; renal tuberculosis, 4 and infarction and carcinoma of

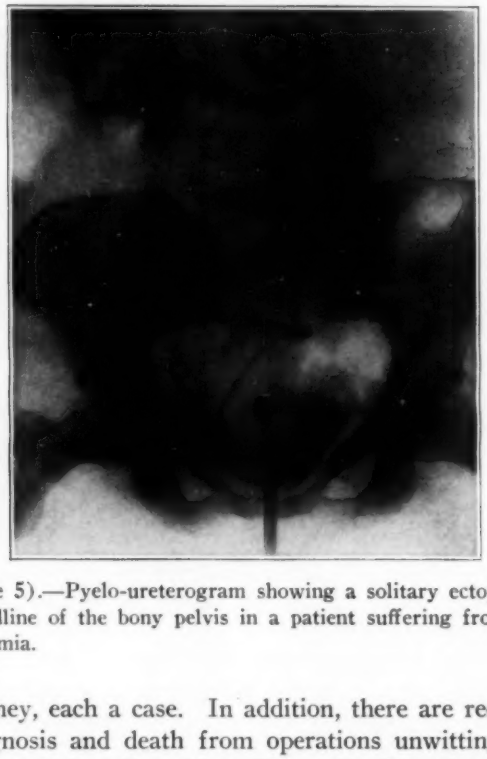


Fig. 16 (case 5).—Pyelo-ureterogram showing a solitary ectopic single kidney lying in the midline of the bony pelvis in a patient suffering from pyelonephritis and chronic uremia.

the single kidney, each a case. In addition, there are records of many errors in diagnosis and death from operations unwittingly performed on the single kidney.[58] Also Young,[59] Eisendrath,[45] Collins,[47]

58. André: Anurie calculeuse dans un rein unique, Ann. d. mal. d. org. génito-urin. **29**:123, 1911. Cathelin: Le rein unique au point de vue chirurgical, Bull. méd. **23**:87, 1909. Eliot: Etiologie, pathogénie, traitement de l'anurie, Thèse de Paris, 1910. Albarran, J.: Néphrectomie dans un rein unique, Assoc. franç. d'urol., Paris, 6th session, p. 133. Guinard: Néphrectomie droite pour pyonéphrose calculeuse, mort: rein unique, Bull. Soc. de chir. de Paris **36**:1077, 1910.

59. Young, H. H.: Young's Practice of Urology, Philadelphia, W. B. Saunders Company, 1926, vol. 2, p. 11.

Ransohoff,[60] Campbell [22] and other writers have cited from the literature 12 deaths following nephrectomy performed on the solitary single kidney.

The solitary single kidney is anatomically and physiologically enlarged, owing mainly to the compensatory functional hypertrophy. The weight of the single organ is approximately double that of a normal kidney, and in view of its having been overworked through carrying on the total excretory function, the organ undergoes a certain degree of degeneration of its elements, ending in a marked degree of hyperplasia. At the same time that it is pathologically enlarged, chronically inflamed and adherent to the surrounding tissue, it becomes painful and exquisitely sensitive to pressure and palpation, giving rise to abdominal symptoms which in many instances have been taken for chronic appendicitis and other conditions erroneously diagnosed.

The single kidney does not eliminate a sufficient amount of urine, and there is evidence of other metabolic disorders of pluriglandular origin, such as cutaneous neurofibromatosis, adiposity, hypertrichosis, cutaneous pigmentation and neurodermatitis. There is marked hypothyroidism, produced in all probability by lack of sufficient elimination and by autointoxication, causing reflex symptoms, hypogenetic function and a chronic uremic condition, in which the patient's body sometimes gives off a strong odor of urine. Obviously the chemical analysis of the blood reveals enormously high figures in the concentration of urea, creatine, creatinine and other constituents. The elements of the urine are also highly concentrated, and the total output is sometimes not even half of what should be eliminated in twenty-four hours.

When the history of a woman of nervous and irritable type is taken and she mentions that she has never menstruated, and when on physical examination absence of external and internal genital organs is observed, then even in advance of urologic examination a diagnosis of congenital absence of one kidney can potentially be made, as in cases 5 and 6 here reported. In case 7, this could be proved cystoscopically and urographically, and in all three cases the diagnosis was confirmed on operation.

These patients suffering from congenital malformation of a solitary single kidney must be treated in a conservative way, both surgically and urologically. In cases in which there is evidence of pyelitis and pyelonephritis with pus in the urine, marked oliguria and other urinary disorders and uremic symptoms, the patient should receive cystoscopic treatments consisting of lavage of the pelvis of the kidney, even using in acute conditions the method of the indwelling ureteral catheter in order to secure drainage and to correct infection. This was done in

60. Ransohoff, J.: Surgery of the Kidney, the Ureter and the Suprarenal Gland, in Keen, W. W.: Surgery, Phildaelphia, W. B. Saunders Company, 1912, vol. 4, p. 200.

case 5 on several occasions, and by this means the patient was saved from fatal uremia.

Operations on the solitary single kidney for removal of stone may be urgently indicated. The most suitable procedure to use, after the kidney or the ureter has been exposed in the usual manner, is either pyelostomy or ureterostomy, which should be regarded as the method of choice. The single kidneys bleed profusely on account of the marked

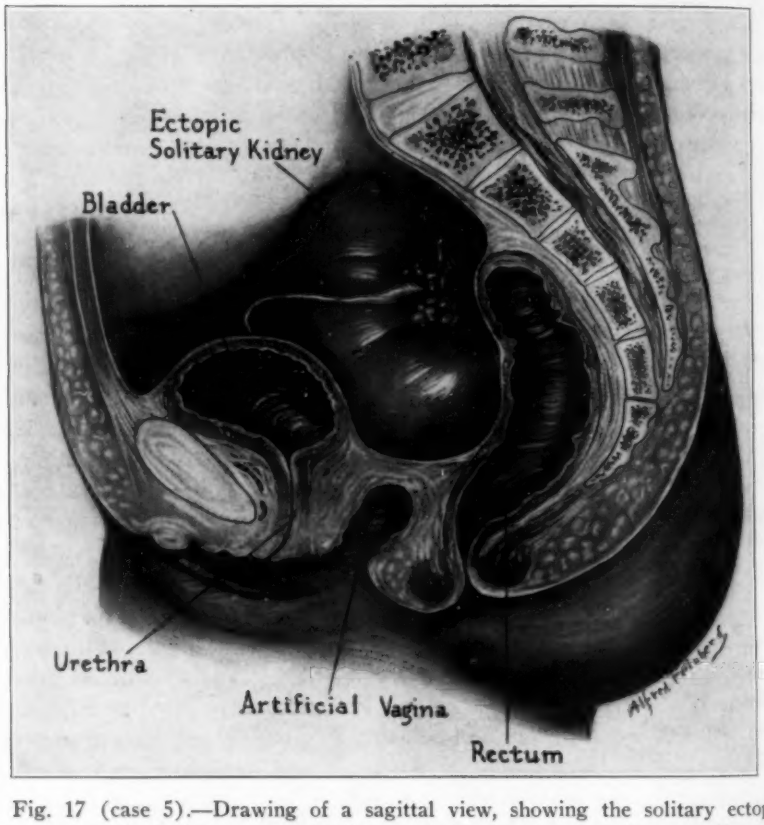


Fig. 17 (case 5).—Drawing of a sagittal view, showing the solitary ectopic single kidney lying between the bladder and the rectum, and also revealing the absence of all genital organs in a patient in whom an artificial vagina had been constructed.

degree of hyperplasia and parenchymatous nephritis present; hence, when nephrotomy or nephrostomy for drainage or for the removal of a stone is done, it should be regarded as a last resort.

Finally, it is essential that, in calculous disease or in anuria of the solitary single kidney, perfect drainage either from below or from above be obtained urologically or surgically, in order to secure the elimination

of urine, thereby assuring the restoration of function and securing preservation of life.

CASE 5.—*Congenital absence of one kidney, the solitary organ being an ectopic single kidney, lying in the midline of the bony pelvis, associated with the congenital absence of vagina and internal genital organs.*

Mrs. E. F., aged 32, was admitted to the ward of the first surgical division of the New York Hospital at midnight of July 11, 1931, in a critical condition. On admission, her chief complaint, she stated, was a pain in the abdomen which she had had for a week and which during the last three days had become very severe, accompanied by nausea, vomiting, dysuria, frequency and burning on urination. The pain was constant and sharp, located in the right lower quadrant and radiating toward the umbilicus and the right lumbar region. She gave a history of having had hematuria several times following an attack of pain; she had also suffered from chronic constipation and had never menstruated.

On physical examination the patient was seen to be an overdeveloped woman for her age, rather obese, chronically ill, with a hypothyroid constitution. The past personal history was of interest. She stated that ten years previously she was operated on for construction of an artificial vagina, and there was a history of her having had two more abdominal operations for adhesions. The vaginal plastic operation was followed by gonorrhea. She has been married twice and has led a very miserable life.

Gynecologic examination showed much congestion and redness of the external genital organs, also scars of the plastic operation; no normal genital organs could be made out. The meatus of the urethra and the clitoris were normal.

Rectal examination revealed no palpable uterus or ovaries, but there was an enlarged tumor mass, rather mobile, which extended up to the umbilicus in the median line and was painful on pressure and free from the rectal wall. With these findings, many tentative diagnoses were made at the time of admission, and the impression was that of an abdominal tumor: (*a*) ovarian cyst, (*b*) fibromyoma of the uterus, or (*c*) retroperitoneal sarcoma.

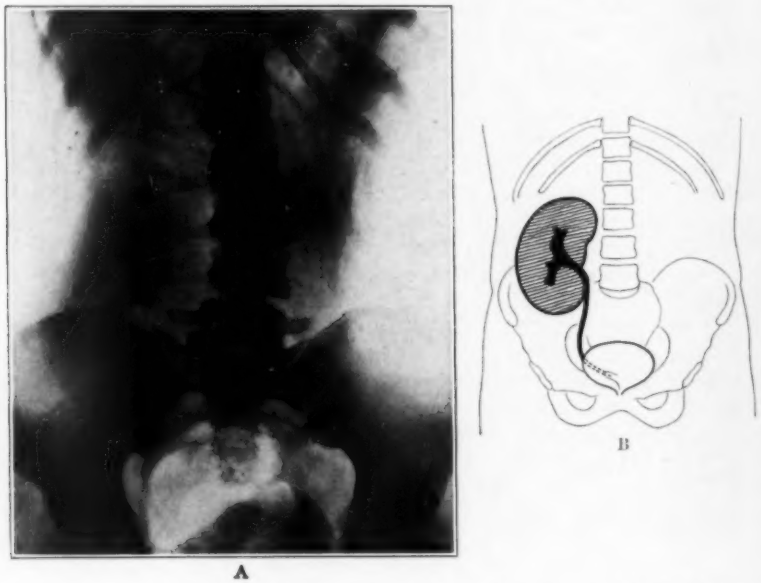
On July 13, cystoscopy was performed. Examination showed a single right ureter with absence of one half of the trigone and the left ureteral orifice. The right ureter was readily catheterized, but the catheter met with an obstruction about 5 cm. from the bladder. Intravenous administration of indigo carmine was then given. Three and one-half minutes after the injection, it appeared from the right kidney, and no excretion was noticed in the bladder, urethra or vagina. It was therefore assumed that the patient had a right solitary kidney. Roentgenograms were taken before and after injection of sodium iodide into the pelvis of the right kidney. A pyelogram revealed an ectopic solitary right kidney. A week later iopax was administered intravenously and a pyelogram confirmed the findings in the other. The patient was discharged from the hospital as improved two weeks later with the advice that she return to the female urologic clinic, where I have been treating her for the last six months. Owing to the anomalous position of the ectopic solitary kidney, she is still suffering from abdominal pains. She is also complaining of chronic uremic symptoms with nausea and vomiting, and has been readmitted twice to the hospital suffering with chronic uremia and acute pyelitis and pyelonephritis; on several occasions an indwelling catheter has been placed in the pelvis of the kidney in order to secure drainage, to correct infection and to relieve the uremic condition.

Meanwhile, she has been having routine cystoscopic treatments in the clinic with lavage of the pelvis of the kidney, which makes her life more comfortable and

relieves her of the urinary symptoms and abdominal pain, allowing the ectopic solitary kidney to exercise a better function and hence preventing the formation of stone or further infection.

CASE 6.—*Congenital solitary ectopic right kidney associated with congenital malformation of the external and internal genital organs.*

Miss F. S., 23 years of age, was referred from the Nursery and Child Hospital for examination on Nov. 4, 1931, by the courtesy of Dr. Kuhner. She had been complaining of pain across the back and also on the lower right quadrant. On physical examination a large palpable tumor mass on the right flank of the abdomen was easily detected. On March 24, 1930, she was operated on in another hospital for chronic appendicitis, at which time an exploratory operation proved the absence of the internal genital organs and revealed a chronic inflamed appendix and

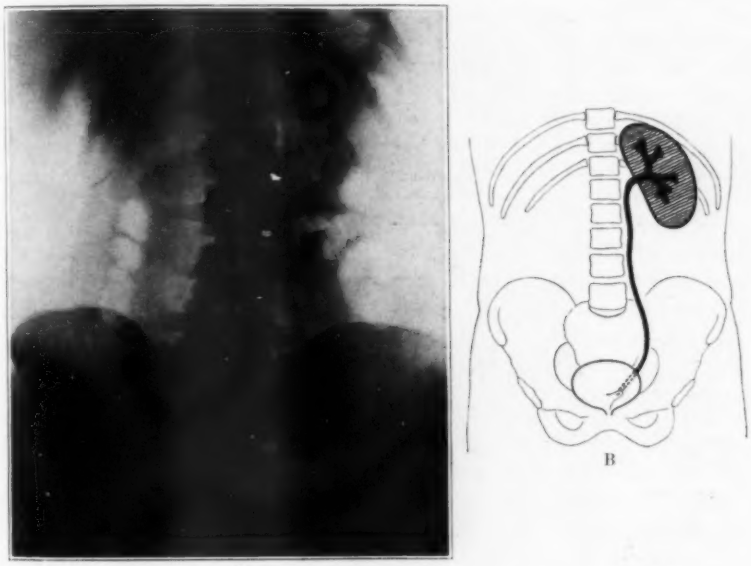


A B

Fig. 18 (case 6).—*A*, pyelogram made following intravenous injection of iopax, revealing the outline of an enormously enlarged solitary ectopic single right kidney. During an exploratory operation for chronic appendicitis the absence of all the genital organs was discovered. *B*, drawing illustrating the position of the ectopic single right kidney, and revealing the coincidence of the congenital absence of one kidney with congenital absence of the vagina.

a retroperitoneal tumor mass, which was believed to be a floating kidney. The patient had no vagina, palpable uterus or ovaries. Although she was well developed for her age, she had never menstruated and had been complaining of slight frequency of urination day and night, with slight dysuria, in addition to the indefinite pain in the lower portion of the abdomen. The physical examination was negative except for the palpable tumor mass on the right side of the abdomen, which was tender on pressure. Analyses of the blood and urine gave negative results. Cystoscopic examination proved the absence of the left side of the trigone, and also the presence of only one ureteral orifice on the right side of the bladder. The single ureter was catheterized, and the urine obtained was clear. Indigo carmine,

given intravenously, appeared in three minutes in the right single kidney. No other indication of blue was seen in the bladder, in the vagina or in the external genital organs. X-ray pictures and pyelograms revealed a single enlarged, hypertrophic and ectopic right kidney, occupying the right lumbo-abdominal-ischial fossa. To ascertain this diagnosis, an intravenous injection of iopax was given a week later, whereupon the pyelogram also confirmed the same discovery—that the left kidney was absent. The right kidney, which was well visualized, showed a marked degree of dystopia and compensatory hypertrophy, thus proving the presence of a solitary congenital ectopic right kidney. There was no shadow indicative of stone anywhere in the urinary tract. A diagnosis was made of congenital absence of one kidney associated with congenital malformation of the external and internal genital organs, and with absence of the vagina. In this case the diagnosis was



A B

Fig. 19 (case 7).—*A*, pyelogram made after the intravenous administration of iopax, revealing an enlarged left single kidney normally placed, in which diagnosis was made cystoscopically, functionally and urographically by both the ascending and descending methods, and was finally confirmed at operation during an exploratory laparotomy for chronic appendicitis. *B*, drawing to illustrate the congenital malformation with absence of the right kidney and of one half of the trigone.

correctly established clinically by the cystoscopic and functional findings as well as by the intravenous method of pyelography, and it was also confirmed by the abdominal exploratory operation.

CASE 7.—*Congenital absence of the right kidney, the left being a solitary hypertrophic organ in normal position; diagnosis made cystoscopically and pyelographically and confirmed at operation.*

Miss E. K., 26 years of age, a private patient of Dr. R. S. Ferguson, by whose courtesy I am reporting this case, was well nourished and well developed. Her chief complaint was an indefinite pain in the abdomen with frequency of urination

during both day and night. She was first seen on March 20, 1930, and cystoscopy was done on April 3. At that time, no right ureteral orifice could be found throughout the bladder, urethra or neck of the bladder. Indigo carmine appeared at the left ureteral orifice three and a half minutes after intravenous injection. No secretion could be observed from the right side of the bladder. A roentgen examination and a pyelogram of the left side revealed the outline of a normally placed left kidney. No renal shadow of the right kidney was visualized. On April 10, cystoscopy was performed again, and when a careful examination of the interior of the bladder failed to reveal any right ureteral orifice, an intravenous injection of iopax was given. The pictures taken showed a normal secretion of the opaque substance in five minutes in the apparently normal left kidney, while on the right side there was no shadow or elimination in several hours. It was, therefore, concluded that there was a congenital absence of the right kidney and a solitary kidney on the left side. No shadow indicative of stone could be seen anywhere in the urinary tract. On June 9, the patient was operated on for a sudden acute attack of appendicitis. At that time a thorough exploration of the right side of the abdomen and the entire pelvis failed to reveal the presence of either a right kidney, a ureter or any rudimentary structures which might be interpreted as belonging to the right half of the urinary tract. The left kidney was palpable and appeared slightly larger than normal. Its position and contour, however, were normal, and the left ureter was also normal. The patient made an uneventful recovery, leaving the hospital in good condition two weeks after the operation. This diagnosis of a congenital absence of the right kidney with a solitary, hypertrophic, single kidney on the left side was made cystoscopically and pyelographically, and was confirmed at operation.

CASE 8.—*Congenital solitary kidney fused in such a manner as to give the impression of being a solitary single organ; ureters in cross ectopic position with the right ureter passing across the midline to reach the solitary double fused kidney; two pelves and two corresponding ureters opening normally into the bladder; diagnosis made roentgenographically and pyelographically in a patient suffering from birth with chronic appendicitis and chronic constipation.*

Miss C. R., aged 24, was admitted into the third surgical division of the New York Hospital on Jan. 7, 1932, and was referred to the urologic department by Dr. W. Cornell. She complained of pain in the right side of the abdomen and stated that for years she had had pain of a recurrent type on the right side. She also gave a history of nausea and vomiting. Three days previously she had a general examination by her family doctor, who advised immediate hospitalization and an operation for the removal of her appendix. Her past history was otherwise irrelevant. She had been constipated all her life and had had to resort to laxatives and enemas. The menstrual and the genito-urinary histories were essentially normal. Apparently she had never had urinary symptoms, although the routine urinalysis during her stay in the hospital showed a cloudy urine, and microscopic examination of the sediments revealed the presence of a few pus cells, for which reason she was advised to have a complete urologic examination before undergoing the operation for the so-called chronic appendicitis. The cystoscopic examination disclosed a normal bladder with two normally placed ureteral orifices. The ureters were catheterized, and the specimen from each kidney was sent to the laboratory for culture estimation of urea and microscopic study. One cubic centimeter of phenolsulphonphthalein, given intravenously, appeared on both sides in two and a half minutes with good concentration. X-ray pictures taken with catheters and instruments in position disclosed the fact that the right catheter, instead of going up into the right lumbar region, passed across the vertebral column to meet with

the kidney of the opposite side. Both catheters were injected with 20 per cent solution of sodium iodide and the pyelograms and pyelo-ureterograms which were taken showed the unusual condition of a fused solitary double kidney with two independent pelves and two ureters opening normally into the urinary bladder. When the diagnosis of this rare congenital malformation of a solitary fused kidney was made, it was believed that, as the right ureter extended across the midline and passed across the great abdominal vessels of the blood, nerve and lymphatic supply, the pressure of these structures interfered with its dynamic contractions and was possibly responsible for the indefinite abdominal symptoms from which the patient had been suffering from birth. It was also noted that there was definite narrowing of the lumen of the right ureter with evidence of pyelitis and pyelonephritis, for which cystoscopic treatments were given, consisting of dilatations of the ureters

Fig. 20 (case 8).—Pyelo-ureterogram, revealing a solitary left fused kidney with two pelves and two ureters in crossed ectopia, both opening normally into the bladder, with pyelitis and pyelonephritis in a patient suffering from so-called chronic appendicitis.

and lavage of the pelvis of the kidney, in order to relieve infection and secure better drainage. The patient was discharged on January 12, unimproved, but before she left the hospital iopax was administered intravenously and a pyelogram was taken which served to confirm the foregoing findings.

Although this case is not the typical picture of congenital absence of one kidney, it is reported here because of its extreme rarity and because the parenchyma of the kidney in itself had assumed such a form and size as to resemble a solitary single kidney; also, because of its surgical and urographic importance for reaching a correct diagnosis

previous to operation. Finally, this case serves to point out that a cystoscopic examination with a differential renal functional test is not sufficient for obtaining a clearcut diagnosis, until roentgenography and urography combined are employed. They are, therefore, of paramount importance to the surgeon, since without them, he may be led to perform an operation in the dark with fatal results.

SUMMARY AND CONCLUSIONS

The study of these three different entities together with the report of two cases of hypoplastic kidney, two of renal aplasia and four of congenital absence of one kidney has served to bring out the confusion that has prevailed in the past and the difficulty in recognizing clinically these three borderline conditions of unique importance in renal surgery.

It has revealed that it is now possible, by means of accurate urologic and urographic examinations, to recognize and differentiate before operation the three conditions of hypoplastic kidney, renal aplasia and congenital absence of one kidney.

The three tables here described not only summarize these conditions but also serve to classify and differentiate them clinically, surgically and anatomopathologically.

In all the eight unusual cases here reported, except case 4, the patients are alive and diagnosis has been made clinically by cystoscopy, by the differential renal functional test and by intravenous and retrograde pyelography; and the diagnosis has also been confirmed at operation in all cases except case 8 in which operation was not indicated.

The etiology underlying these malformations of the kidney must be conceived as based on a congenital defect of embryonic origin, in which an arrest of development has occurred during the cycle of embryonic life. The failure of the wolffian duct of the mesonephros to give off a renal bud is responsible for the presence of total agenesis and for the multiplicity of varieties of kidney malformations that are commonly found during life or at postmortem examination.

The recognition of the hypoplastic kidney is of extreme importance to the urologist and the surgeon, because it is obviously well demonstrated that when nephrectomy is done in its mate for associated pathologic process, the infantile or hypoplastic kidney is incapable of undergoing compensatory functional hypertrophy in order to sustain life.

In the hypoplastic kidney the ureter is always patent, and the excretory function is present. The renal function is diminished in regard to the estimation of urea and elimination of phenolsulphonphthalein, although the excretion of indigo carmine may appear to be within normal limits. The diagnosis must, therefore, be based on pyelographic data.

The condition of renal aplasia is mainly characterized by an arrest of embryonic development in which the kidney has never been formed and the amorphous renal mass has no eliminatory function, while the ureter, although opening into the bladder, is not patent and is accordingly devoid of function.

The diagnosis of renal aplasia can be readily made cystoscopically and pyelographically by combining the use of the retrograde and the intravenous method of pyelography. The histologic sections made of the specimens removed at operation or at postmortem examination reveal the presence of rudimentary renal tissue characterized by an embryonic type of glomeruli and tubules, as can be seen in the two cases here reported (cases 3 and 4).

These two conditions of hypoplasia and aplasia must not, however, be confused with secondary renal atrophy or the destruction of one kidney due mainly to disease or an associated pathologic process of long standing. In the latter condition, the kidney undergoes complete destruction; its parenchyma degenerates and its cortical and medullary substance are lost, as has been commonly observed in the autonephrectomy produced by renal tuberculosis, nephro-ureterolithiasis and other types of lesions. This condition can also be produced experimentally, which is obviously not the case with the entities just described.

The treatment of unilateral hypoplastic kidney and renal aplasia is surgical and consists of the removal of the infantile organ or the amorphous rudimentary mass of tissue, provided the kidney of the opposite side is compensatorily hypertrophied and is performing enough function to sustain life.

The congenital absence of one kidney is differentiated from hypoplastic kidney and renal aplasia by the total absence of nephrogenic tissue on the one side and hence by the complete absence of the corresponding ureter and kidney, and of one half of the trigone, on the same side. It is also important to note that the suprarenal gland on the agenetic side is likewise commonly absent, which is not the case in renal aplasia or hypoplastic kidney.

The solitary kidney may be found in ectopic or cross ectopic position, and is characterized by having a single ureter opening into the bladder. It should be differentiated from that type of renal fusion in which the solitary fused organ has two pelves and two ureters opening independently into the bladder.

The coincidence of renal and genital anomalies is greater than has been suspected, and suggests that when there is a congenital malformation of the genital organs, particularly in the female, the great probability is that there is also lack of development of nephrogenic tissue and hence of one of the twin renal organs, as in cases 5 and 6.

The recognition of solitary single kidney requires careful scrutiny both clinically and at operation, and even at autopsy. Many cases are

recorded in the literature as total unilateral agenesis in which there is, in fact, evidence of the presence of nephrogenic tissue in the agenetic side of the body. The classification and differentiation now presented tend to separate clinico-anatomopathologically these three borderline conditions, which have been the subject of much confusion in the past.

The solitary single kidney is peculiarly subject to disease and in that event carries a fatal prognosis. The association of a pathologic process —parenchymatous nephritis, stone formation, pyelitis and pyelonephritis with a tendency to hydronephrosis, oliguria, infection, anuria and death— has been commonly recorded in the literature. Through errors in diagnosis many operations have unwittingly been performed on the solitary single kidney followed rapidly by anuria and death. In these modern days of exquisite accuracy in the urologic and urographic diagnosis, no operation should ever be performed on either kidney without previous assurance of the presence of its fellow.

The symptomatology of the three conditions under discussion is insidious. The presence of bilateral abdominal pain with an enlarged palpable mass in one side of the abdomen, may signify hypertrophy of one kidney and demands a careful urologic investigation of the upper urinary tract. Nevertheless, sole reliance should not be placed on the intravenous urographic findings, despite the brilliancy of the achievements of this new method, for it cannot be too strongly emphasized that in many cases retrograde bilateral pyelograms are indispensable.

The localization of a pathologic process or disease of the kidney or ureter on the one side does not exclude the necessity of complete investigation of the opposite side also.

Anomalies of the upper urinary tract are commonly met with in this urographic era, and whenever present should be regarded as potentially surgical, in view of their liability to cause stagnation of urine, infection and loss of function, resulting in serious pathologic conditions.

The congenital absence of one kidney does not incapacitate its owner for the normal physiologic functions of life. According to recent statistics, patients with a solitary single kidney live an average of from thirty-five to forty years, and the cause of death may be disease totally unrelated to the genito-urinary tract.

40 East Sixty-First Street.

ABSTRACT OF DISCUSSION

DR. C. L. PEACOCK, New Orleans: Dr. Gutierrez's classification is a most excellent one and, so far as I know, the only one in literature differentiating hypoplasia, aplasia and agenesis. One point should be emphasized, and that is the importance in renal surgery, and the necessity, of bilateral pyelograms and kidney functional tests.

DR. THOMAS D. MOORE, Memphis, Tenn.: It is not uncommon for the question to arise as to whether one is dealing with the congenital absence of a kidney.

In a case recently reported the following data seemed to indicate a left renal agenesis: The patient was a young woman who had a right hydronephrosis of 240 cc. capacity; there was no objective evidence of a left ureteral orifice; intravenous injections of indigo carmine and phenolsulphonphthalein appeared from the right orifice only; excretion urography disclosed no evidence of the media in the region of the left kidney; a catheter passed to the right kidney and left in situ for a period of seventy-two hours took care of the entire amount of urine excreted, none being voided about the catheter as would have occurred with a functioning left kidney. In the roentgenogram there was no evidence of a left renal shadow. On physical examination a kidney could not be palpated on the left side. The right hydronephrosis responded in a satisfactory way to a pyelo-ureteroplasty. In another case, however, essentially the same data were obtained, except that the absence of the right kidney was indicated and on the left side a pyonephrosis was superimposed on a renal neoplasm terminating fatally. Necropsy disclosed the error of the assumption that there was a congenital absence of the right kidney; the organ was a mere shell of almost paper thinness and filled with about 100 cc. of thin cloudy fluid. This case illustrates how easily one can be mistaken in the diagnosis of renal agenesis and the necessity of a direct anatomic observation of the renal area, either by surgical exploration or by necropsy, before the positive statement is justified that there is congenital absence of a kidney.

Excretion urography has proved to be of value in the diagnosis of renal aplasia. Recently a small rudimentary kidney was demonstrated by this means; definite compensatory hypertrophy had occurred in the opposite organ.

DR. I. G. DUNCAN, Memphis, Tenn.: I wish to report a case which I believe to be one of congenital absence of a kidney.

The patient was a young white woman, aged 26, who had always menstruated very scantily and irregularly. She came to the gynecologic service of the Baptist Hospital. At operation it was found that the left side of the uterus was undeveloped. There was no tube or ovary on the left side. Following the operation urinary difficulties had developed. I was called in consultation. Cystoscopy was done and it was found that the left side of the bladder was undeveloped. There was no sign of the ureteral ridge or of an orifice. The right side was normal. We injected indigo carmine intravenously and watched carefully. A strong dye came down on the right side but none whatsoever from the left side of the bladder. Later we made intravenous injections of skiodan. No dye showed on the left side, but a large hypertrophied kidney was demonstrated on the right. It is my impression that the left kidney was absent. The pain was on the right side and the trouble seemed to be of a pyelitic nature. Since no operation was performed, we cannot say positively whether there was a total absence, but by all the means used we were unable to demonstrate the presence of kidney tissue on that side.

DR. THOMAS D. MOORE, Memphis, Tenn.: Dr. Gutierrez pointed out the differential diagnosis of aplasia and agenesis in an interesting and clear way. We cannot be 100 per cent sure until necropsy is performed. In one case, that of a young woman, there was no shadow on the roentgenogram; by urographic examination, no medium appeared in the left kidney; on functional tests, no dye appeared on the left side, and no kidney was palpable on physical examination. On those findings it was concluded that no kidney was present on the left side. This patient made an excellent recovery following pyeloplasty, but it was not known positively whether she had a solitary kidney.

In another case there was no evidence of a kidney on the right, although all the methods of examination were carried out that were used in the first case. That patient died, and on necropsy a mere shell of a kidney was found on the

right, where it had been assumed that there was a solitary kidney. The bag was of almost tissue paper texture, and there was no function remaining. This shows how mistaken one can be in these cases.

I wish to emphasize the value of urography in demonstrating these findings. In a recent case a small rudimentary kidney was demonstrated quickly by this method.

Dr. H. W. E. Walther, New Orleans: I have had one case of infantile kidney. The patient was a girl of 17 who was beginning her university work and was the captain of her basketball team. She was driven to seek medical relief because of intense pain in the right lumbar region. Urography revealed an infantile kidney. Nephrectomy was done and she was completely relieved. She had been studied by several physicians and had been told that if she wore a belt and stopped athletics she would be all right. She did not feel that she wanted to give up her activities, and as we had a high percentage of phenolsulphonphthalein from the opposite side and a zero reading from the painful side it was thought best to operate.

I wish to ask Dr. Gutierrez if, in these infantile kidneys, intense pain is a prominent symptom.

Dr. Robert Gutierrez, New York: Dr. Walther is correct. In hypoplastic kidney the predominating symptom is pain on the side where the lesion is established. This is well explained both pathologically and physiologically. Due to lack of development, the kidney is diminutive or rudimentary in size. The pelvis is small, the emptying time is greatly diminished and retention is produced. Thus, sooner or later, a hydronephrotic crisis gradually develops. As this hypoplastic kidney is incapacitated for sustaining life, it is most important, when nephrectomy is to be done on the opposite side, that the condition be urographically recognized before operation. At no time has such a kidney been larger than when first discovered. It is, therefore, a true congenital lack of development. As infection results from lack of drainage and proper function, the only correct indication is nephrectomy, provided that the lesion is unilateral and that the kidney on the opposite side is normal or functioning sufficiently to sustain life.

I have observed in renal aplasia that the aberrant, functionless mass of renal tissue also produces the characteristic pain in the side. The proper indication is an exploratory lumbotomy in order to remove the aberrant renal tissue. Only by a complete urologic and urographic examination can a definite diagnosis be reached and these two conditions of hypoplastic kidney and renal aplasia be properly differentiated.

The literature has reported many cases of congenital absence of one kidney, in which at postmortem examination a mass of aberrant renal tissue has been discovered on the side opposite to the supposedly solitary organ. This anatomic or histopathologic observation obviously revealed the presence of nephrogenic tissue, which in turn proved the true existence of a hypoplastic or aplastic kidney. A study of these cases has disclosed the frequency of coincidental congenital malformations of the genital tract, particularly in the female.

I wish to place special emphasis on the importance of taking bilateral pyelograms, when a congenital malformation of the upper urinary tract is suspected. Renal tests alone are often misleading in the diagnosis. Recently one of our colleagues reported a case in which nephrectomy was done for infected hydronephrosis. The patient died a few days later in an uremic coma. At postmortem examination a hypoplastic kidney was found, proving that the kidney, although having a certain amount of function, was incapable of undergoing the compensatory hypertrophy necessary to sustain life.

The purpose of my presentation has been primarily to draw attention to these three hazardous conditions of the kidney, so commonly confused in the literature, and to offer a method of proper differentiation, recognition and classification of these three unique conditions. With this object in view, I have drawn up the three tables, which I have just shown.

Do not overlook the possibility of these pathologic and unique conditions of the kidney, for such an oversight may not only mislead in the diagnosis but also result in a fatal prognosis. I wish you the best of luck in properly recognizing these conditions since otherwise you may encounter the sad experience of having removed a solitary single kidney.

SWEAT GLAND TUMOR

KELLOGG SPEED, M.D.
CHICAGO

Mrs. M. C., 34 years old, was admitted to the Presbyterian Hospital on April 19, 1932, and was discharged on April 25, 1932. Her complaint on admission was of a tumor on the anterior surface of the proximal half of the left thigh, present since birth as nearly as she knew, and of varicose veins in the left leg which had been present for about two years.

The tumor on the thigh had always been painless, except when traumatized, as it often was when in her occupation as housewife the patient was cooking or working at a table. These irritations were repeated many times a day until the central portion of the tumor had been worn away, leaving an ulcerated mass about 7 cm. wide in its longest axis surrounded by a raised ring of tissue 3 cm. wide, which near the border was white and hard and blended somewhat abruptly into the surrounding skin. The patient had of recent years been unable to wear stockings which covered the tumor, and in place of the conventional garter fastened to her corset above she wore a circular elastic band to hold up the stocking on that leg. This band was very tight and was believed to be the cause of the varicose veins in the left leg. There were no similarly enlarged veins in the right leg.

The tumor undoubtedly had its origin in early infancy, and its growth had been steady ever since it was first noticed, its relative size compared to that of the thigh remaining about the same. It had not undergone any sudden increase in size or any rapid change in appearance, and caused little pain until it was bumped.

The past history included no information connected with the tumor. Physical examination showed a well developed normal woman. The surface of the tumor was purple with a white border, and the red, raw surface of the upper central portion had been ulcerated and was slightly infected (fig. 1 *A*). As a whole, the growth was freely movable in the deeper tissues on the thigh. Its exact size was 10 by 5 by 3 cm. There was a small painless adenopathy in the left femoral region. All laboratory examinations of blood, urine and blood pressure gave normal results. The gross appearance and hardness of this tumor made a diagnosis of a very slowly growing epithelioma with an ulcerated surface the most plausible one, and yet the long history, only partly supported by the adenopathy in the groin, was contraindicative of this conclusion.

On April 20, 1932, a biopsy was made, and immediate frozen sections showed the tissue to be taken from a sweat gland tumor. A 7 inch (17.78 cm.) elliptic incision was then made about the tumor down through the subcutaneous fat, a generous margin of skin being taken beyond the growth. Although the fascia lata appeared not to be penetrated, part of it underlying the tumor mass was excised, and the tumor was removed in one piece (fig. 1 *B*). The rent in the fascia lata was closed with a continuous catgut suture, and the skin was drawn together by three silkworm gut button retention sutures with black silk interrupted in the edge of skin. A twisted silkworm gut drain was left in the central part of the wound. The adenopathy in the groin was believed to be the result of absorption from the ulcerated surface on that thigh, and no attempt was made to excise it.

The wound healed rather slowly, discharging considerable oily serum, but closed without infection.

Sweat gland tumors are rare; they are often confused with malignant tumors elsewhere on the body, as in the breast or on the face and neck, and seem to be unknown on the lower extremities. The first description was by Werthen,[1] and the technical name of naevus syringoadenomatosus papilliferus was applied. Prior to 1925 there were less than twenty-five instances recorded in the literature. In that year Arzt and Kumer [2] reported three cases.

The first patient was a woman, 25 years of age, who presented a tumor 5 by 11 cm., raised from 2 to 3 cm. above the surface of the temple. The growth was somewhat fungating and lobulated, with a warty surface resembling that of a papilloma of the genitalia. It was soft and reddish, and had been present since birth. It had been growing during the last three years. Histologically, it was a cystic structure with papillomatous ingrowth. In these cysts there was an eosinophilic mass with cells in various stages of degeneration. In many places the cysts

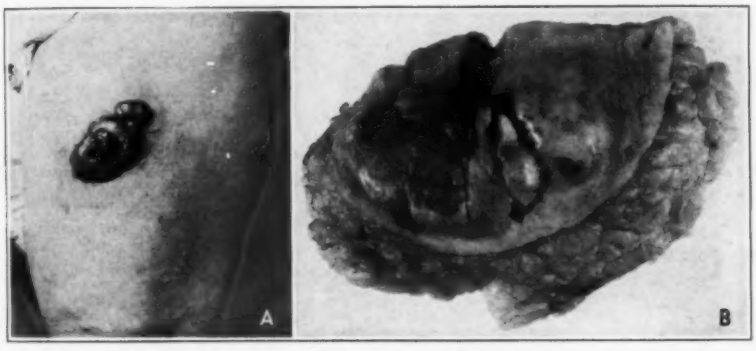


Fig. 1.—*A*, the tumor on the left thigh, present since birth. The raised surface and ulcerated central portion with a sharp demarcation from surrounding skin are noteworthy points. *B*, the specimen after its removal with underlying fat. Portions have been excised for biopsy and microscopic study. The raised and ulcerated surface appears like that of an epithelioma.

were connected by strands of cells with the surface epithelium. Many plasma cells were present.

The second patient was a girl of 17 who had a tumor that had been present since birth on the parietal region of the scalp; it was 2 by 8 cm., with a papillary raised surface resembling that of a condyloma. The growth was excised and did not recur. Histologically, there were numerous branched strands of cells, as well as tubules, some narrow and some dilated, with a basal layer of cuboidal cells and an inner layer of cylindric cells. The tumor cells were surrounded by an infiltrate of plasma cells, and there was a papillary ingrowth into the lumen of some of them. They were connected with the epidermis in many places. Sebaceous glands

1. Werthen, cited by Gans: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 2, p. 282.

2. Arzt, L., and Kumer, L.: Ueber Drusennaevi, Arch. Dermat. u. Syph. **148**:323, 1925.

were present in the outer cutis and sweat glands in the deeper cutis. Some of the latter were cystic, but there was no evidence of papillary ingrowth.

The third patient was a girl of 12, whose scalp had been burned with hot water, leaving a scaly and papillomatous tumor which increased in size and looked like a condyloma. Histologically, the structure was about the same as in the first case.

Pick believes that all these tumors are the result of congenital disturbance of the sweat gland anlage, and so they are nevi. It is difficult to determine from what part of the ectoderm they take their origin. Two main views are offered. The first, supported by Kreibich, is that the tumor cells take their origin from hair anlage. The second,

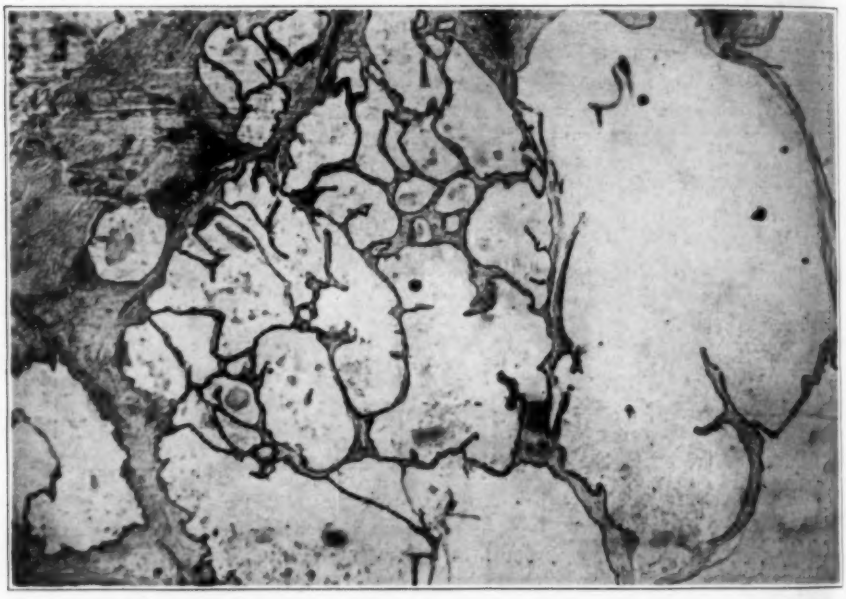


Fig. 2.—Section through part of the specimen, showing the cystlike spaces with some papillomatous ingrowth from the lining walls. The cysts vary in size. Some of them are distinctly tubular in their proliferation.

supported by the majority of authors, is that they take their origin from sweat gland anlage. As a matter of fact, the germinal layer of epithelium has a power of developing sweat glands, hair or sebaceous glands. It is from this germinal epithelium that the tumor cells originate. Consequently, they may have the power to develop any of these structures.

In 1926, Biberstein [3] reported three cases.

3. Biberstein, Hans: Ueber Papilliforme Syringo-Cystadenome, Arch. Dermat. u. Syph. **152**:602, 1926.

The first patient was a woman, 45 years old, presenting a growth on the scalp the size of a large coin, with papillary excrescences; it had been present since birth. The growth was partially epithelialized and partially eroded and granulated. Histologic examination of the tumor showed that it was made up of loose stroma of connective tissue cells. The surface covered one or two layers of cylindric cells, and from this surface epithelial cords ran downward. In places these were hollowed out to form tubules. They branched and intertwined, forming a complicated structure. The tubules were lined with two layers of epithelium, and from this arose papilliform projections into the lumen. The spaces in the stroma were closely packed with plasma cells. There were no hairs, sebaceous glands or normal sweat ducts.

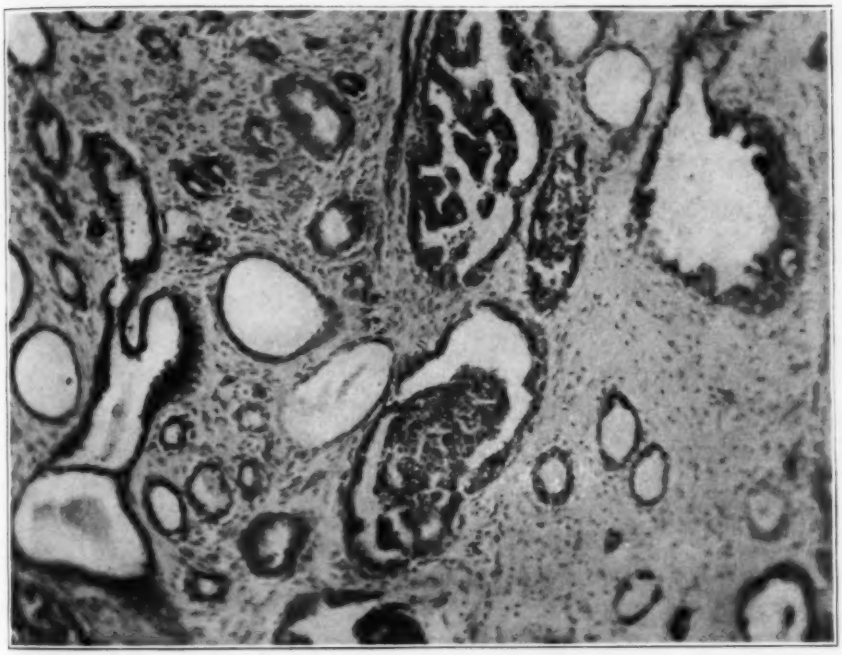


Fig. 3.—Section through another portion of the specimen, showing the papillary proliferation of the tubule and cyst lining, which in some instances nearly fills the lumen. Deeply staining plasmocytes in the surrounding tissues are characteristic. There is no definite evidence of malignancy.

The second patient was a woman of 29, who had a tumor in the scalp which had been present for three years. It was coin-sized, flat and slightly raised, with a morulated surface and papillary projections from the surface. Histologically, it was similar to the tumor in the first case, except that there were normal sweat glands in the corium beneath the tumor, and in two instances these sweat glands showed a definite tendency to proliferation.

The third patient was a girl of 11 years who presented a tumor on the left side of the thorax of three years' duration. The growth was a flat, round nodule the size of a finger-nail; it had a warty surface, and the color resembled that of

lupus vulgaris. Histologically, the tumor was made up of tubules and cysts with ingrowing papillomatous proliferation of epithelium. These were surrounded by plasma cell infiltrates. The large cystic areas were connected with deeper lying sweat ducts which were larger than normal, the epithelial lining of which had a tendency to bud into the lumen.

These tumors are clinical and histologic entities, because the epithelium that lines the cysts and tubules proliferates into the lumen in the form of simple or much branched papillae resembling papillary

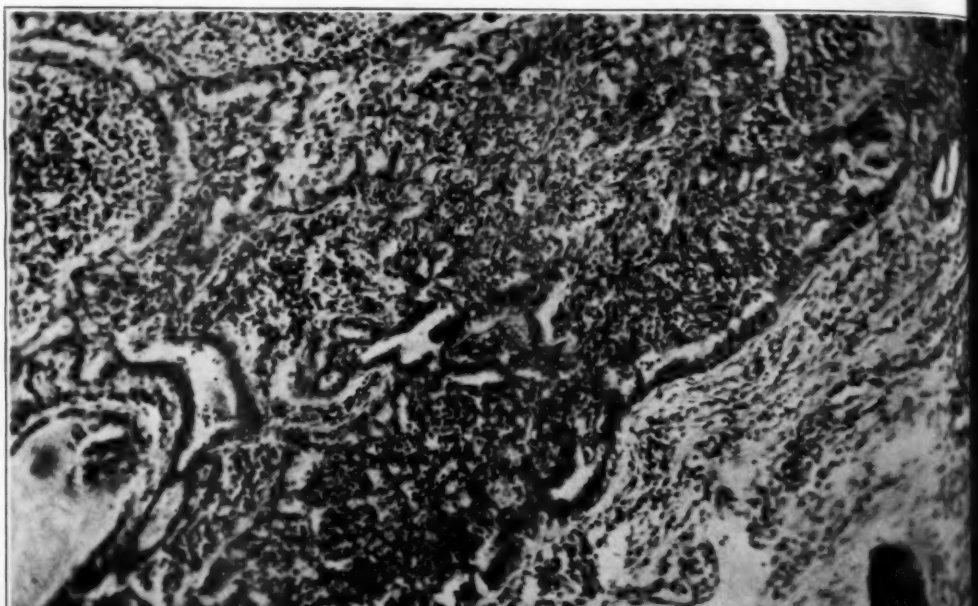


Fig. 4.—Section cut through the long axis of a tubule which appears as a sweat gland. The lumen is filled with the proliferated lining and a mass of cell detritus. Plasmocyte cells are numerous and characteristic. The tumor is evidently benign.

cystadenoma of the ovary or breast. This papillary ingrowth differentiates the tumors from simple hydrocystomas on one hand and from tubular cystadenomas of the vulva on the other hand. The structure is so characteristic that it cannot be mistaken histologically (figs. 2, 3 and 4).

The typical tumor of which the one shown in the illustrations is an example is chiefly made up of cystic, dilated tubules. About the

tumor cells may be found typical nevus cells in some instances and usually large numbers of well developed plasma cells. Malignant transformation of this adenoma is possible and has been reported by Hedinger. In the lumen of the cystic structure, between the papillomatous excrescences, one finds cell detritus and a sort of slime which reminds one of the material found in simple sweat gland adenomas.

The interesting points in the literature and their relation to clinical diagnosis, especially when the tumor involves the breast, have been summarized by Biberstein:

1. The location of the tumor mass may be either in the very superficial part of the skin or may be deep in the cutis.

2. The content of the cysts is colloidal in some cases; in others it is a fine, granular, homogeneous, eosinophilic mass.

3. Branches have been described, which when present form tubules. These may be in part solid strands or cords of cells and in part tubules.

4. Papillary excrescences of the inner wall into the lumen of the tubules or the cysts are often found, as in intracanalicular papillomas. These were present in most of the cases reported, and at times there were excretory ducts which opened on the surface.

5. Solid strands of cells may be made up of cells of basal cell type, of flat epithelial cells or, as in some cases in the literature, of cells which resemble sebaceous gland cells.

6. There is more or less dense accumulation of plasma cells.

7. Lymphocytic infiltration may be present, but is usually only perivascular.

8. The membrana propria is usually evident in places around cysts, tubules and strands.

9. The general relation of the tumor to the epidermis is often confusing. The strands of the tubules may be connected with epidermis or may even open into it. The cysts may open directly into the epidermis in some cases or through ducts in others, or broad, solid bands of cells may connect the cysts with the epidermis. The tubules may be connected with the epidermis in a similar variety of fashions.

10. The relation of the tumor tissue to sweat glands and to hairs is as follows: (*a*) In one case in the literature the excretory duct apparently opened into the hair follicle. Hair and sebaceous glands may be entirely lacking in the tumor, hair anlage with cysts may be present, or there may be well formed hairs. A sebaceous transformation of some simple cells of the tumor occurred in Krebich's case.

(*b*) The sweat glands in Biberstein's three cases were connected with the tumor mass. Unassailable evidence of the connection of the tumor cells with normal sweat glands has been made the basis of calling them sweat gland adenomas by Bartels, Brocq and others. Adenoma-like proliferation of the dilated sweat glands may occur beneath the tumor tissue. Other authors have described transformations from dilated sweat glands to cysts of the type seen in these tumors.

Biberstein believes that these growths are undoubtedly sweat gland tumors, but whether they are adenomas or epitheliomas is a subject of argument. The presence of plasma cells is an evidence of a marked tendency to proliferation, as well as their occurrence at certain ages; whether the tumors are derived from already developed sweat glands or from their anlage cannot be determined.

INFLUENCE OF HYPERTONIC SALT SOLUTIONS ON THE MOTILITY OF NORMAL AND OF OBSTRUCTED INTESTINE

AN EXPERIMENTAL STUDY

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I. M. GAGE, M.D.

AND

R. A. CUTTING, M.D.

NEW ORLEANS

Since the original observations by Hughson and Scarff [1] in 1924 that the intravenous administration of hypertonic sodium chloride solutions increased intestinal movement, these solutions have been employed extensively by clinicians in the treatment of adynamic ileus. Beneficial results obtained by the use of hypertonic sodium chloride solutions have been reported by a number of investigators.[2] In a previous

From the Department of Surgery, Tulane University School of Medicine.

1. Hughson, W., and Scarff, J. E.: Influence of Intravenous Sodium Chloride on Intestinal Absorption and Peristalsis, Bull. Johns Hopkins Hosp. **35**:197, 1924.

2. (*a*) Ross, J. W.: Hypertonic Saline in Adynamic Ileus, Canad. M. A. J. **16**:24, 1921. (*b*) Coleman, E. P.: Further Observations on Use of Hypertonic Saline Solution in Acute Intestinal Obstruction, Anesth. & Analg. **6**:210, 1927. (*c*) Gosset, A.; Binet, L., and Petit-Dutaillis, D.: Toxemia in Intestinal Obstruction: Experimental and Clinical Study, J. de chir. **35**:321, 1930. (*d*) Duncombe, M.: Postoperative Intestinal Occlusion Treated by Ileocolostomy and Intravenous Injections of Hypertonic Salt Solution, Bull. et mém. Soc. nat. de Chir. **54**:1482, 1926. (*e*) Courty, L.: Postoperative Intestinal Occlusion Treated with Intravenous Injections of Hypertonic Salt Solutions, ibid. **55**:602, 1929; Acute Intestinal Occlusion Treated by Cecal Anus and Injection of Hypertonic Salt Solution, ibid. **54**:1450, 1928; Four Cases of Intestinal Occlusion Treated by Deviation and Intravenous Injections of Hypertonic Salt Solution with "Solu-Camphor," ibid. **55**:1335, 1929. (*f*) Lion, R.: Une observation d'intoxication par occlusion intestinal haute, guérie par injections de chlorure de sodium à haute dose, suivies d'opération, Bull. et mém. Soc. de chir. de Paris **21**:141, 1928 (*g*) Kuss, G.: A propos des injections de sérum salé hypertonique par voie rectale dans l'occlusion intestinale, Bull. et mém. Soc. nat. de chir. **54**:1460, 1928. (*h*) Szuve, in discussion on Duncombe: Postoperative Intestinal Occlusion Treated by Ileocolostomy and Intravenous Injections of Hypertonic Salt Solution, ibid. **54**:1482, 1928. (*i*) Battista, A.: Use of Hypertonic Saline Solution in Intoxication Caused by Acute Obstruction, Riforma med. **49**:905, 1929. (*j*) Dreyer, H. B., and Tsung, Thelma: Effect on Intestinal Movements of Certain Salts Administered Intravenously, J. Pharmacol. & Exper. Therap. **36**:629, 1929. (*k*) Tytgat: Employment of Hypertonic Sodium Chloride Solutions in Intestinal Occlusion, Ann. et bull. Soc. roy. de méd de Gand **8**:146, 1929. (*l*) Clement, F.: Un cas d'iléus post-opératoire traité

investigation,[3] we demonstrated that hypertonic sodium chloride solutions definitely increased intestinal activity. Orr [4] has emphasized the importance of the administration of hypertonic salt solutions (20 cc. of a 10 per cent and 500 cc. of a 5 per cent sodium chloride solution) in the treatment of postoperative gas pains. Reid,[5] working with a Thiry-Vella fistula of the jejunum, showed that the intravenous administration of hypertonic sodium chloride solution not only increased the activity of an intestinal segment but also increased the propulsive type of motility.

In order to determine the effect of various hypertonic salt solutions on the motility of the intestine, the present investigation was undertaken. One hundred and twenty-eight observations concerning the effect of the intravenous injection of salt solutions on the movement of the intestine were made in sixty-five dogs. Of this group, only one hundred and seventeen are used in the present study because in eight a physiologic Ringer's solution was employed, and in three the results obtained could not be used because of a leak in the intestinal balloon. In the three latter cases, there undoubtedly occurred an increase in peristalsis and propulsive activity as evidenced by copious evacuation of the intestinal contents through the enterostomy tube, but because the effect could not be measured the results are not included. Ten observations were made on normal animals, thirteen on animals with twenty-four hour intestinal obstruction, forty-nine on animals with forty-eight hour obstruction and forty-five on animals with seventy-two hour obstruction. In each instance, kymographic tracings were made of the intestinal movements, and the results herein presented are based on an analysis of these kymographic tracings and are not dependent on mere unaided ocular

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avec succes par injections intravéineuses de solution hypertonique de chlorure de sodium, Bull. et mém. Soc. d. chirurgiens de Paris **22**:347, 1930. (*m*) Bojovitch, V.: Traitement des occlusions intestinales post-opératoires, Presse méd. **38**:1662, 1930. (*n*) Denis, R.: Indications, mode d'action et posologie des injections de chlorure de sodium hypertonique dans l'occlusion intestinale, ibid. **38**:203, 1930; A propos des récentes discussions sur le rôle du chlorure de sodium hypertonique dans l'occlusion intestinale, ibid. **38**:906, 1930. (*o*) Dogliotti, A. M., and Mairano, M.: Notre expérience de trois années dans la thérapeutique salie dans l'occlusion intestinale, ibid. **38**:880, 1930. (*p*) Prati, M.: Intestinal Obstruction: Good Results with Large Doses of Sodium Chloride, Riv. di pat. sper. **5**:168, 1930. (*q*) Barthelemy: Accidents d'occlusion post-opératoire; injections de sérum salé hypertonique, Bull. et mém. Soc. nat. de chir. **56**:637, 1930. (*r*) Bouisset, L., and Fabre, P.: Peristalsis in Obstruction; Action of Sodium Chloride, Compt. rend. Soc. de biol. **104**:847, 1930.

3. Ochsner, Alton; Gage, I. M., and Cutting, R. A.: The Value of Drugs in the Relief of Ileus, Arch. Surg. **21**:924 (Dec.) 1930.

4. Orr, T. G.: The Action of Sodium Chloride upon the Small Intestine, Ann. Surg. **94**:732, 1931.

5. Reid, P. E.: Effect of Hypertonic Sodium Chloride Intravenously on Intestinal Peristalsis, Proc. Soc. Exper. Biol. & Med. **29**:220 (Nov.) 1931.

observations. Concomitant respiratory, and in the majority of instances, concomitant blood pressure, tracings were made. In thirty-eight blood pressure tracings were not obtained, because the observations were made on "survival" animals so that exposure and sacrifice of one of the larger arteries was not feasible. In the majority of instances (seventy-nine), observations were made on anesthetized (barbital) animals, the abdomens of which were open and submerged in warm physiologic solution of sodium chloride, as described by Sanders [6] and Alvarez,[7] and as previously used by us.[8] This method will subsequently be referred to as the "open abdomen" technic. In thirty-eight instances, observations were made on unanesthetized "survival" animals according to the "closed abdomen" technic, which is published in detail elsewhere.[9]

It is briefly as follows:

At laparotomy, the terminal ileum is divided and each end inverted and closed. Approximately 5 cm. proximal to the lower end of the upper segment, a fenestrated enterostomy tube is introduced through a stab wound, the enterostomy tube extending proximally into the lumen of the bowel for a distance of about 20 cm. Approximately 5 cm. proximal to this enterostomy opening, a rubber tube carrying a balloon is introduced proximally into the lumen of the bowel for a distance of from 5 to 10 cm. Both of these tubes are brought out through the omentum and abdominal wall, following which the latter is closed. The enterostomy tube is left open. After twenty-four hours with the enterostomy tube still open, the tube carrying the balloon is attached to a Maury tambour and a kymographic tracing taken of the normal intestinal movement, before, during and after the intravenous injection of saline solution. The enterostomy tube is then tied off, producing an intestinal obstruction. After varying periods of time, usually at twenty-four, forty-eight and seventy-two hour intervals, observations concerning the effect of the intravenous injection of hypertonic salt solutions on the intestinal activity are made. The following solutions were used for intravenous injection: sodium chloride solution, 20 per cent; "hypertonic" Ringer's solution; "hypertonic" Hartmann's combined solution; sodium chloride, 20 per cent, and calcium chloride, 0.5 per cent; and sodium chloride, 20 per cent, and potassium chloride, 0.5 per cent.

HYPERTONIC SODIUM CHLORIDE SOLUTION

Twenty-four observations were made concerning the effect of 20 per cent sodium chloride on obstructed intestine. In seventeen, the obstruction had existed forty-eight hours, whereas in seven, it had

6. Sanders, H.: Ezn. Methode tot onderzoek der peristaltische Bewegingen van het darmkanaal, enz. Voorloop. mededeel, abstr., Centralbl. f. d. med., Wissensch., 1871, p. 479; cited by Alvarez.[7]

7. Alvarez, W. C.: The Mechanics of the Digestive Tract, New York, Paul B. Hoeber, Inc., 1929.

8. Ochsner, Alton; Gage, I. M., and Cutting, R. A.: Comparative Value of Splanchnic and Spinal Analgesia in the Treatment of Experimental Ileus, Arch. Surg. **20**:802 (May) 1930.

9. Gage, I. M.; Ochsner, Alton, and Cutting, R. A.: Effect of Insulin and Dextrose on the Normal and the Obstructed Intestine, Arch. Surg. **26**:658 (April) 1933.

existed seventy-two hours. Three observations (previously referred to) made in one animal are unreliable, because the tracing showed that a leaky intestinal balloon was present, even though the intestine was active as evidenced by copious evacuation of feces through the enterostomy tube. These three observations are omitted because of the inability to measure accurately the effects produced by hypertonic saline solution. In three other instances, there was evidence of a leaky balloon, but the results are included even though the values obtained are probably lower than the true values. The amounts of the hypertonic sodium chloride solution which were administered varied from 2.7 to 10.2 cc., the average being 8.4 cc. per kilogram of body weight. The average amounts administered to animals with forty-eight hour and with seventy-two hour obstructions were 8.7 and 6.2 cc. per kilogram of body weight, respectively. There was an average increase in blood pressure

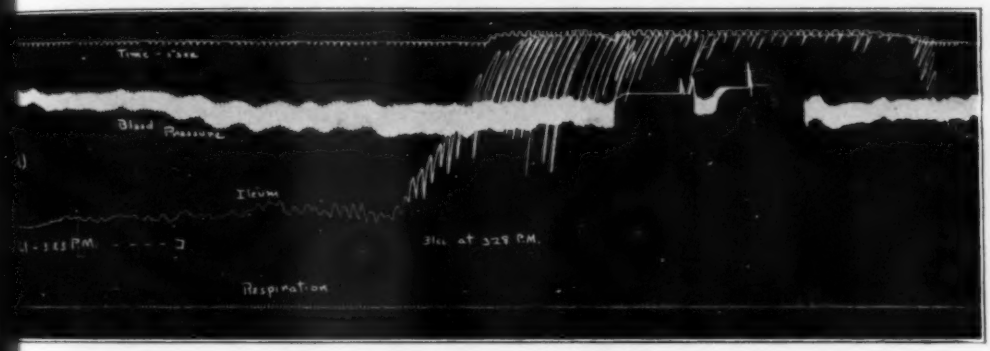

Fig. 1.—Kymographic tracing showing the effect on seventy-two hour obstructed intestine of the intravenous injection of 20 per cent sodium chloride. As shown at the left of the tracing, there was little or no movement of the intestine. Shortly after the beginning of the infusion, there was some activity followed by a marked increase in tone and also an increase in amplitude, the lever almost passing off the drum (open abdomen technic).

of 22 mm. of mercury in 23.5 per cent of the animals with forty-eight hour obstruction. In 64.8 per cent, there was no change in blood pressure; in 5.8 per cent, there was a temporary fall in pressure, and in 5.8 per cent, there was a sustained decrease of 20 mm. of mercury. In all of the animals with seventy-two hour obstruction that received the hypertonic sodium chloride solution, there occurred no change in blood pressure. Of all the animals (both with forty-eight hour and seventy-two hour obstructions) that received 20 per cent sodium chloride solution the blood pressure was increased in 20 per cent (an average increase of 22 mm. of mercury), unchanged in 70 per cent, temporarily decreased in 5 per cent and definitely decreased in 5 per cent. Of the twenty-one observations made following the intravenous administration of 20 per

cent sodium chloride solution, the intestinal activity was increased in nineteen (90.4 per cent), unchanged in one (4.7 per cent) and decreased in one (4.7 per cent). The average increases in intestinal tone and amplitude of intestinal movement in the nineteen in which there was an increased activity were 28.6 and 5.05 mm., respectively. In two instances, there were increases in amplitude of intestinal movement but no associated increases in tone, and in two other instances, there were increases in tone which were not associated with increases in amplitude. The increases in intestinal tone varied from 7 to 80+ mm. The increases in amplitude varied from 0.5 to 40 mm. The average duration of the increased intestinal activity was 11.1 minutes. Of the nineteen observations in which there occurred an increase in intestinal activity, sixteen were made in animals with forty-eight hour obstruction and three in

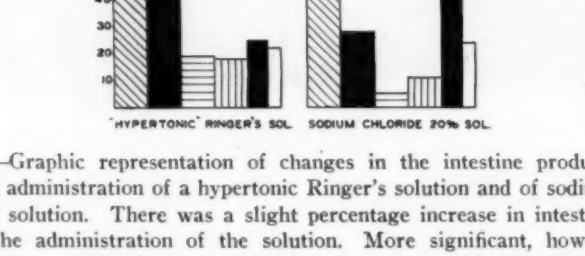

Fig. 2.—Graphic representation of changes in the intestine produced by the intravenous administration of a hypertonic Ringer's solution and of sodium chloride, 20 per cent solution. There was a slight percentage increase in intestinal activity following the administration of the solution. More significant, however, is the character of the change in that the intravenous injection of a hypertonic Ringer's solution produced a much greater increase in tone (solid black), increase in amplitude, and a longer duration of the activity than did sodium chloride, in spite of the fact that the dose of the hypertonic Ringer's solution was less than that of the sodium chloride solution. In the other graphs the various columns denote the same thing.

animals with seventy-two hour obstruction. The average increases in intestinal tone and amplitude in the animals with forty-eight hour obstruction were 20.56 and 2.25 mm., respectively. The average increases in tone and amplitude in those with seventy-two hour obstruction were 71.6 and 20 mm., respectively (fig. 1). The average durations of the increased intestinal activities in animals with forty-eight and the seventy-two hour obstructions were five and twenty-one minutes, respectively. In the one instance (4.7 per cent) in which there

occurred a decreased activity, the tone was decreased 11 mm., but there was no change in the amplitude of intestinal movement (fig. 2, table 1).

"HYPERTONIC" RINGER'S SOLUTION

Sixty-one observations were made concerning the effect of intravenous administration of a hypertonic Ringer's solution on normal and obstructed intestine. The expression hypertonic Ringer's solution is obviously incorrect as Ringer's solution is a physiologic solution. The hypertonic solution used, however, was obtained by multiplying quantities of salts contained in Ringer's solution by 20. The solution so obtained contained: sodium chloride, 18 per cent; calcium chloride, 0.52 per cent, and potassium chloride, 0.6 per cent. In forty-three instances, the open abdomen technic was used and in seventeen instances, the closed abdomen technic. As the results obtained with

TABLE 1.—*Sodium Chloride 20 Per Cent; Open Abdomen Experiments*

	Total Observations	Normal Intestine	24 Hour Obstruction	48 Hour Obstruction	72 Hour Obstruction
Number of observations	21	....	....	17	4
Average dose per Kg. of body weight, cc.	8.4	....	....	8.7	6.2
Average blood chloride before, mg. per 100 cc.	653.5	....	....	657.3	638
Average blood chloride after, mg. per 100 cc.	804	....	....	802.7	809
Increase in blood chloride, per cent	23.1	....	....	22.1	26.8
Increased intestinal activity, per cent	90.4	....	....	94.1	75
No change in intestinal activity, per cent	4.7	....	....	5.8	0
Decreased intestinal activity, per cent	4.7	....	....	0	25
Average increase in tone, mm.	28.6	....	....	20.5	71.6
Average increase in amplitude, mm	5.05	....	....	2.25	20
Average duration increased activity, minutes	11.1	....	....	5	21

the closed abdomen experiments differed from those obtained with the open abdomen experiments, the two will be considered separately (fig. 3). Of the forty-three observations made following the intravenous administration of the hypertonic Ringer's solution in which the open abdomen technic was used, fourteen observations were made on animals with forty-eight hour obstructions and twenty-nine on animals with seventy-two hour obstructions. The amounts of the hypertonic Ringer's solution administered varied from 0.6 to 6 cc., the average being 2.5 per kilogram of body weight. The average amount of the hypertonic Ringer's solution administered to the animals with forty-eight hour obstructions was 2.6 cc., whereas those with seventy-two hour obstructions received an average amount of 2.48 cc. per kilogram of body weight. Intravenous injection of the hypertonic Ringer's solution into animals with forty-eight hour obstruction produced an increase in blood pressure in 20.8 per cent, no change in 50 per cent and temporary but slight falls in blood pressure varying from 8 to 30 mm. of mercury (the average 18.8 mm. of mercury) in 28.2 per cent. In 80

per cent of the observations made on animals with seventy-two hour obstruction, there were increases in blood pressure varying from 10 to 30 mm. of mercury, the average being 17.5 mm. of mercury. In 10 per cent, there was no change, and in 10 per cent, there were slight but temporary decreases in blood pressure. In 38.4 per cent of all animals that received the hypertonic Ringer's solution, there were increases in blood pressure, the average being 18 mm. of mercury. In 38.4 per cent, there was no change, and in 23.5 per cent, there were temporary but slight falls in blood pressure. The blood chloride values before the administration of the hypertonic Ringer's solution varied from 554 to 759 mg., the average being 629.8 mg. per hundred cubic centimeters. The blood chloride values after the administration of the solution varied from 721 to 825 mg., the average being 771.2 mg. per hundred cubic centimeters, an average percentage increase in blood chlorides of 22.5. The average blood chloride values before and after the intravenous

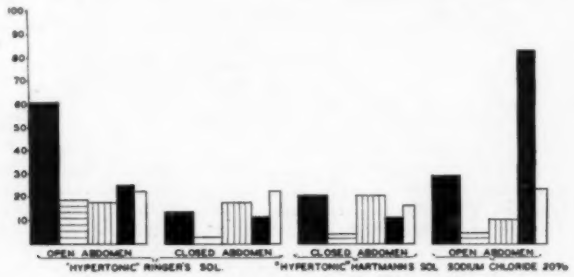

Fig. 3.—Graphic representation of the effect on the intestine of the intravenous administration of a hypertonic Ringer's solution, a hypertonic Hartmann's solution, and of sodium chloride, 20 per cent. A comparison of the results obtained by the open abdomen and closed abdomen technics is made with the hypertonic Ringer's solution. The hypertonic Hartmann's solution (closed abdomen technic) caused a slightly greater increase in intestinal activity than did the hypertonic Ringer's solution (closed abdomen technic).

administration of the hypertonic Ringer's solution in the animals with forty-eight hour obstructions were 659.5 and 785.42 mg. per hundred cubic centimeters, respectively. The average percentage increase in blood chlorides in this group was 19.2. The average blood chloride values before and after the administration of the hypertonic Ringer's solution in the animals with seventy-two hour obstruction were 611.2 and 761.3 mg. per hundred cubic centimeters, respectively, an average percentage increase of 24.5. Of the entire group of forty-three, forty-one (95.3 per cent) showed an increase in intestinal activity, whereas only two (4.7 per cent) showed no change. In one of these, the Ringer's solution was given at the height of the intestinal activity from a previous injection. If this one exception is eliminated, stimulation of the intestinal activity occurred thirty-seven times out of thirty-eight

observations (97.7 per cent). The average increases in intestinal tone and amplitude of movement were 63.8 and 16.07 mm., respectively. The increases in tone varied from 5 to 125 mm., and the increases in amplitude ranged from 2 to 150 mm. The average duration of the increased intestinal activity was eighteen minutes (fig. 2). The increases in tone were probably actually greater than indicated by these figures, because in four instances (all in the group with seventy-two hour obstruction) the true responses are not expressed because of a leaky intestinal balloon. Also, in three instances, the tracing needle passed off the kymographic drum and the true value could not be measured. The true average duration of increased activity was undoubtedly longer than eighteen minutes, because in seven of the forty-three instances, the intestine was still active at the time the observations were terminated.

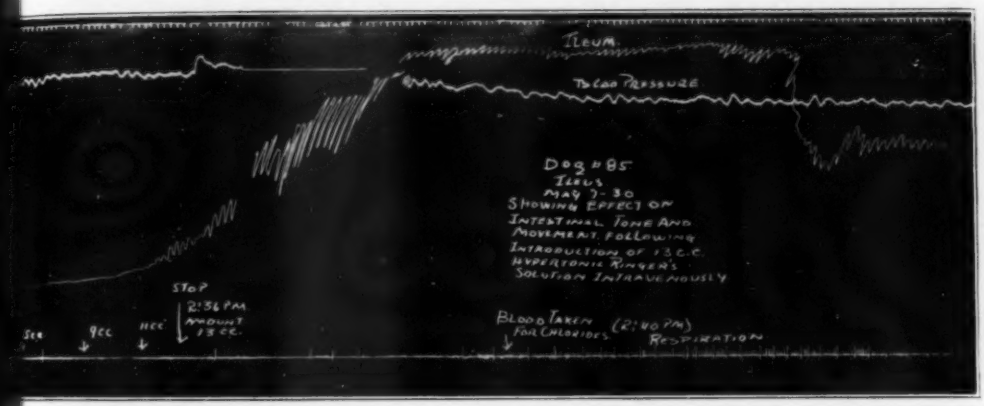

Fig. 4.—Kymographic tracing showing the effect on forty-eight hour obstructed intestine of the intravenous injection of a hypertonic Ringer's solution. At the extreme left of the tracing, the intestine was inactive. After 11 cc. of the solution had been given, there was a rapid rise in intestinal tone associated with an increase in intestinal movement, following which the intestine became more or less spastic. This increased activity was continued throughout the experiment although there was a moderate fall in tone after approximately eight minutes (open abdomen technic).

The average increases in intestinal tone and amplitude which occurred in animals with forty-eight hour obstructions were 62.1 and 11.3 mm., respectively (fig. 4). The average duration of the increased activity was 12.4 minutes. The average increases in tone and amplitude of the intestine of the animals with seventy-two hour obstructions were 64.2 and 18.3 mm., respectively (figs. 5 and 6). The average duration of the increased activity was 20.36 minutes (table 2).

Eighteen observations concerning the effect of the intravenous administration of the hypertonic Ringer's solution on normal and

obstructed intestine of unanesthetized animals with the closed abdomen technic were made. The amount of Ringer's solution administered intravenously varied from 0.7 to 1.7 cc., the average being 1.17 cc. per kilogram of body weight. The blood chloride values before the administration of the hypertonic Ringer's solution varied from 510 to 640 mg., with an average of 588 mg. per hundred cubic centimeters. The blood

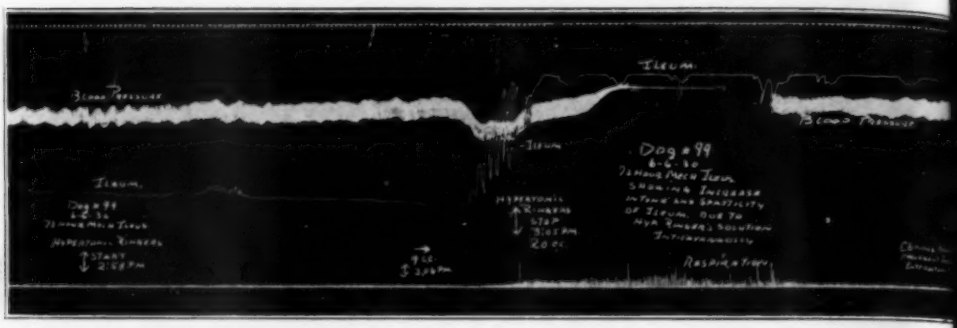

Fig. 5.—Kymographic tracing showing the effect on seventy-two hour obstructed intestine of the intravenous administration of a hypertonic Ringer's solution. There was some activity in the intestine before the administration of the solution, as evidenced by periodic movement of the intestine. Following the administration of the solution, there was a marked rise in intestinal tone, which in the beginning was associated with an increased intestinal movement. This was, however, followed by a sustained tone. During this period there was copious evacuation of feces through the enterostomy tube (open abdomen technic).

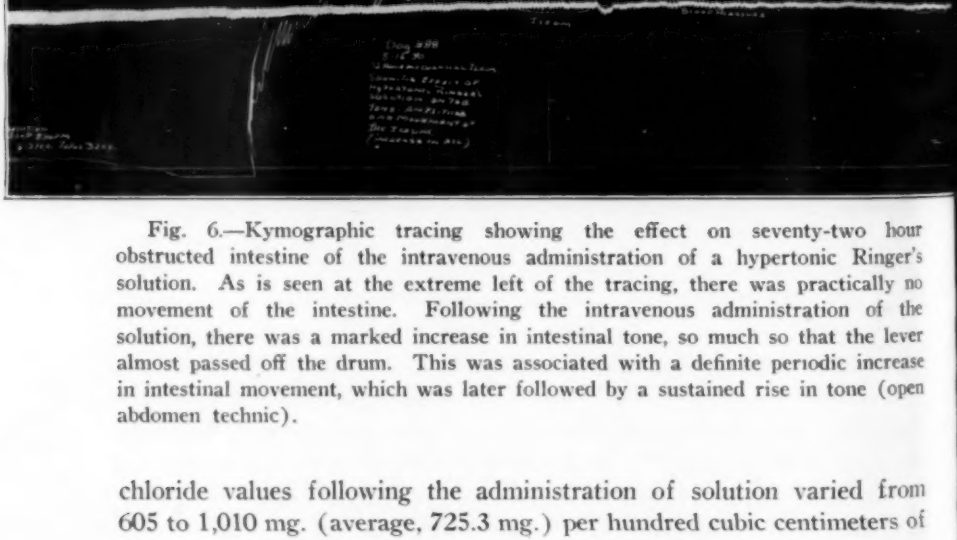

Fig. 6.—Kymographic tracing showing the effect on seventy-two hour obstructed intestine of the intravenous administration of a hypertonic Ringer's solution. As is seen at the extreme left of the tracing, there was practically no movement of the intestine. Following the intravenous administration of the solution, there was a marked increase in intestinal tone, so much so that the lever almost passed off the drum. This was associated with a definite periodic increase in intestinal movement, which was later followed by a sustained rise in tone (open abdomen technic).

chloride values following the administration of solution varied from 605 to 1,010 mg. (average, 725.3 mg.) per hundred cubic centimeters of

blood. There was an average percentage increase in blood chlorides of 23.4. Of the eighteen observations, three were made on normal intestine, six on intestine which had been obstructed for twenty-four hours, six on intestine which had been obstructed for forty-eight hours and three on intestine which had been obstructed for seventy-two hours. Of the entire group, there was an increase in intestinal activity in seventeen (95 per cent), whereas in one (5 per cent) no change occurred. In those instances in which increased activity occurred, there were average increases in tone and amplitude of 13.1 and 2.9 mm., respectively. The average duration of the increased intestinal activity was 17.6 minutes (fig. 7). In three observations made on normal intestine following intravenous injection of the hypertonic Ringer's solution, there was an

TABLE 2.—*Hypertonic Ringer's Solution; Open Abdomen Experiments*

	Total Observations	Normal Intestine	24 Hour Obstruction	48 Hour Obstruction	72 Hour Obstruction
Number of observations	43	....	....	14	20
Average dose per Kg. of body weight, cc	2.59	....	....	2.6	2.48
Average blood chloride before, mg. per 100 cc	629.8	....	....	659.5	611.2
Average blood chloride after, mg. per 100 cc	771.2	....	....	785.4	761.3
Increase in blood chlorides, per cent	22.5	....	....	19.2	24.5
Increased intestinal activity, per cent	97.7	....	....	92.8	100
No change in intestinal activity, per cent	2.3	....	....	7.17	0
Decreased intestinal activity	0	....	....	0	0
Average increase in tone, mm	63.8	....	....	62.15	64.6
Average increase in amplitude, mm	16.07	....	....	11.3	18.3
Average duration of increased activity, mm	18	....	....	12.4	20.38

increase in activity in two (66.6 per cent) and no change in one (33.3 per cent). In the latter instance, however, the Ringer's solution was given at the height of intestinal activity, which had been produced by a previous injection of the solution. The average increases in tone and amplitude in this group were 11.5 and 5 mm., respectively. The average duration of the activity was thirty-two minutes. In all (100 per cent) of the six observations made on animals with twenty-four hour obstructions there were increases in intestinal activity, the increases in tone and amplitude being 5.8 and 2.3 mm., respectively (fig. 8). The average duration of the increased activity was 14.3 minutes. In all (100 per cent) of the six animals with forty-eight hour obstructions, there were increases in the intestinal activity following the intravenous administration of the hypertonic Ringer's solution. The increases in tone and amplitude were 23.3 and 3.3 mm., respectively (fig. 9). The average duration of the increased activity was more than fourteen minutes. In the three observations made on the seventy-two hour obstructed intestine, there was an increased activity in all with average increases in tone

and amplitude of 30 and 2 mm., respectively (fig. 10). The average duration of the increased activity was 22.3 minutes (table 3).

Thirty-four observations were made concerning the coagulation of the blood of animals with intestinal obstruction. Twenty-six of these were made before and after the administration of the hypertonic Ringer's solution, whereas in eight, the observations preceded and followed the administration of morphine. In the latter group, it was found that the average coagulation time before the administration of morphine was two minutes and forty-eight seconds, whereas the average coagulation time following the administration of morphine was two minutes and twenty-five seconds, an average decrease in coagulation time of 13.6 per cent. In all instances in which the coagulation time was determined before and after the intravenous administration of the hypertonic Ringer's solution, there was a decreased coagulation time (increased

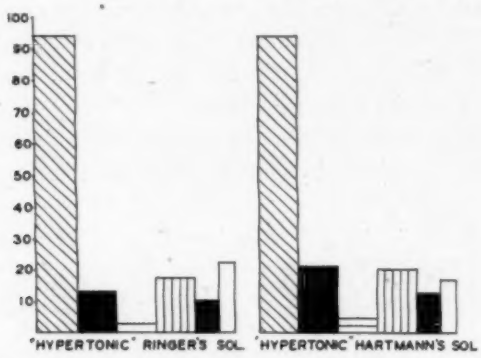

Fig. 7.—Graphic representation showing the effect on intestinal activity of the intravenous administration of a hypertonic Ringer's solution and of a hypertonic Hartmann's solution. The percentage increases in intestinal activity are approximately the same; there are, however, slightly greater increases in tone and in amplitude of movement following the hypertonic Hartmann's solution than that obtained with the hypertonic Ringer's solution.

TABLE 3.—*Hypertonic Ringer's Solution; Closed Abdomen Experiments*

	Total Observations	Normal Intestine	24 Hour Obstruction	48 Hour Obstruction	72 Hour Obstruction
Number of observations	18	3	6	6	3
Average dose per Kg. of body weight, cc.	1.17	1.09	1.02	1.08	1.16
Average blood chloride before, mg. per 100 cc.	588.93	607.3	589.1	557	590.5
Average blood chloride after, mg. per 100 cc.	725.3	666.6	728.3	792.5	670
Increase in blood chloride, per cent	23.4	9.4	26.8	42.2	12.7
Increased intestinal activity, per cent	94.4	66	100	100	100
No change in intestinal activity, per cent	5.5	33*	0	0	0
Decreased intestinal activity	0	0	0	0	0
Average increase in tone, mm.	13.1	4.5	5.8	23.3	30
Average increase in amplitude, mm.	2.9	5	2.3	3.3	2
Average duration of increased activity, minutes	17.6	32	14.3	14+	22.3

* Ringer's solution given at height of activity following previous injection.

coagulability of the blood) following the administration of the solution. The percentage decreases in coagulation time varied from 12.7 to 57, the average coagulation time before and after intravenous injection being two minutes and fifty-four seconds and one minute and fifty-six seconds, respectively, an average percentage decrease of 33.

Fig. 8.—Kymographic tracing showing the effect on twenty-four hour obstructed intestine of the intravenous administration of a hypertonic Ringer's solution. As seen at the extreme left of the tracing, there was no activity in the intestine, but following the administration of the solution, there was an increase in intestinal tone and also amplitude of movement. This increase in intestinal movement showed evidence of periodicity (closed abdomen technic).

Fig. 9.—Kymographic tracing showing the effect on forty-eight hour obstructed intestine of the intravenous administration of a hypertonic Ringer's solution. Following the infusion, there was a marked increase in intestinal tone associated with an irregular increase in intestinal movement. This increased activity persisted a relatively short time (closed abdomen technic).

In eight instances in which an intravenous injection of a normal Ringer's solution was made into normal animals, there was an increase

in intestinal activity in four (50 per cent) and no change in four (50 per cent). The average increases in tone and amplitude were 35.5 and 2.2 mm., respectively (fig. 11). The average duration of the increased activity was 21.6 minutes.

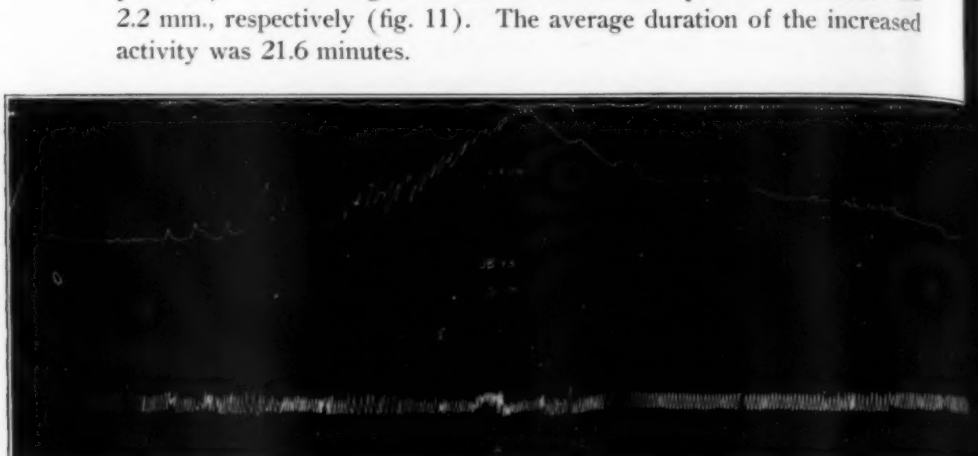

Fig. 10.—Kymographic tracing showing the effect on seventy-two hour obstructed intestine of the intravenous administration of a hypertonic Ringer's solution There was a marked increase in intestinal tone which was associated with an increase in intestinal movement. The duration of the increased activity was short (closed abdomen technic).

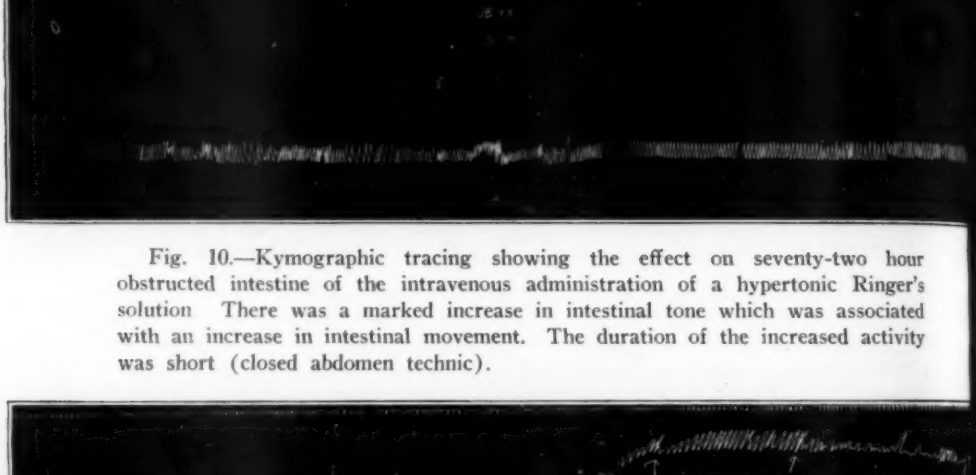

Fig. 11.—Kymographic tracing illustrating the effect on normal intestine of the intravenous injection of a physiologic Ringer's solution. As seen in about the midportion of the tracing, there occurred following the intravenous administration of 40 cc. of the solution a rapid rise in intestinal tone which was associated with an increase in intestinal movement. During this period of increased activity, the kymographic drum was stopped, the entire period of increased activity being one hour and ten minutes (closed abdomen technic).

"HYPERTONIC" HARTMANN'S COMBINED SOLUTION

Twenty observations concerning the effect of the intravenous injection of hypertonic combined solution of Hartmann were made on

animals, the closed abdomen technic being employed. Hartmann's solution [10] is a modified Ringer's solution containing the electrolytes of the blood and also sodium lactate, which is readily oxidized. The solution as now employed by Hartmann is as follows:

Sodium lactate	2.80	Gm. per liter
Sodium chloride	5.85	Gm. per liter
Potassium chloride	0.373	Gm. per liter
Calcium chloride	0.274	Gm. per liter

As this solution is being dispensed in a concentrated form in ampules, which facilitates its use, it was thought advisable to test its efficacy in stimulating the intestine. The solution as dispensed is diluted twenty-five times in order to make a physiologic solution. In our experiments, we added to the contents of a 20 cc. ampule, 5 cc. of sterile distilled water, giving a solution with the following constituents:

Sodium chloride	11.7	per cent
Sodium lactate	5.6	per cent
Potassium chloride	0.74	per cent
Calcium chloride	0.54	per cent

The amount of the hypertonic Hartmann's solution which was administered varied from 0.18 to 3.2 cc., the average being 1.16 cc. per kilogram of body weight. Blood chloride values before the administration of the solution varied from 476 to 725 mg. with an average of 547.63 mg. per hundred cubic centimeters of blood. The blood chloride values after the administration of the solution varied from 500 to 780 mg., the average being 670.79 mg. per hundred cubic centimeters. There was an average percentage increase in blood chlorides of 16.3. The average amount of the hypertonic Hartmann's solution administered to animals with normal intestine was 1.1 cc. per kilogram of body weight. The average blood chloride values before and after the administration of the solution were 564.28 and 632 mg. per hundred cubic centimeters, respectively, an average percentage increase of 12.2. The average amount of the hypertonic Hartmann's solution administered to animals with twenty-four hour obstructions was 1.4 cc. per kilogram of body weight. The average blood chloride values before and after the administration of this solution were 539.83 and 645 mg. per hundred cubic centimeters of blood, respectively, an average percentage increase of 19.8. The average amount of Hartmann's solution administered to animals with forty-eight hour obstructions was 0.9 cc. per kilogram of body weight. The average blood chloride values before and after the administration of the solution were 712.5 and 739 mg. per hundred cubic centimeters, respectively, an average percentage increase of 3.9.

10. The Hartmann's solution was supplied us by the Eli Lilly Company.

The amount of Hartmann's solution administered to animals with seventy-two hour obstructions was 0.98 cc. per kilogram of body weight. The average blood chloride values before and after the administration of the solution were 672.75 and 745.77, respectively, an average percentage increase of 10.8. Of the twenty observations, in nineteen (95 per cent) there were increases in intestinal activity following the intravenous administration of the hypertonic Hartmann's solution. In only one instance (5 per cent) was there no change in intestinal movement. The average increases in tone and amplitude in the nineteen instances were 20 and 3.6 mm., respectively; the average duration of the increased intestinal activity was 20.2 minutes (figs. 3 and 7). Seven of the twenty observations were made on normal intestine. In 87.5 per cent of these

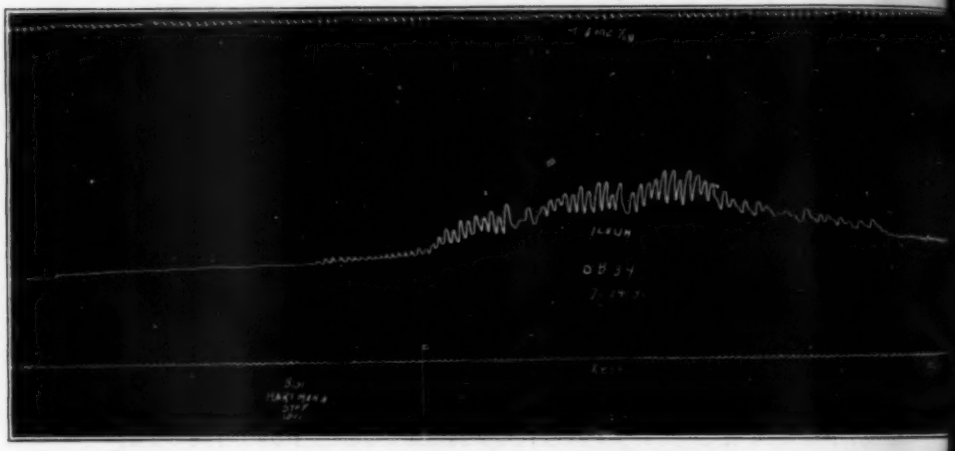

Fig. 12.—Kymographic tracing showing the effect on normal intestine of the intravenous administration of a hypertonic Hartmann's solution. As illustrated at the extreme left of the tracing, there was little movement of the intestine. Following the infusion of the solution, there was a moderate rise in intestinal tone associated, however, with a very definite increase in intestinal movement (closed abdomen technic).

there was an increase in intestinal activity, whereas in 12.5 per cent there was no change. The average increases in tone and amplitude in this group were 25.6 and 3 mm., respectively, the average duration of the activity being 20.4+ minutes (fig. 12). Seven observations were made on animals with twenty-four hour obstruction, in all (100 per cent) of which there was an increase in intestinal activity. The increases in tone and amplitude were 16.2 and 1.7 mm., respectively (fig. 13). The average duration of the activity was 17.2+ minutes. Both of the observations made concerning the effect of the hypertonic Hartmann's solution on forty-eight hour intestinal obstruction showed an increase

in intestinal activity, the increases in tone and amplitude being 28 and 8.5 mm., respectively (fig. 14). The average duration of the increased activity was 16.5 minutes. In four observations made on seventy-two hour obstructed intestine, there was an increase in intestinal activity

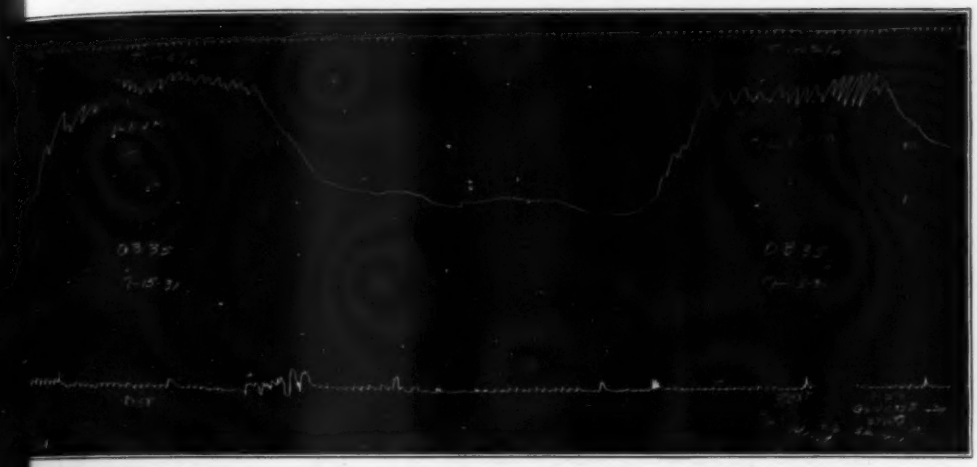

Fig. 13.—Kymographic tracing showing the effect on twenty-four hour obstructed intestine of the intravenous administration of a hypertonic Hartmann's solution which had been given twenty-five minutes previously. As illustrated, there were periodic increases in intestinal activity, consisting of increases in tone and amplitude of intestinal movement (closed abdomen technic).

Fig. 14.—Kymographic tracing illustrating the effect on forty-eight hour obstructed intestine of the intravenous administration of a hypertonic Hartmann's solution. There was a slight rise in intestinal tone but a definite increase in amplitude of intestinal movement (closed abdomen technic).

in all. There were increases in tone and amplitude of 13.5 and 5 mm., respectively (fig. 15). The average duration of this increased activity was 28.2 minutes (table 4).

SODIUM CHLORIDE, 20 PER CENT; CALCIUM CHLORIDE, 5 PER CENT

Four observations concerning the effect of the intravenous injection of sodium chloride, 20 per cent, and calcium chloride, 5 per cent, were made on animals with forty-eight hour intestinal obstruction. The amounts injected varied from 2.2 to 4.4 cc., the average being 2.7 cc. per kilogram of body weight. The average blood chloride values before and after the administration of the hypertonic salt solution were 616.2 and 816 mg., respectively, an average percentage increase of 32.5. There were increases in intestinal activity in all instances (100 per cent). The average increases in intestinal tone and amplitude were 25.7 and 12.5 mm., respectively (fig. 16). The duration of the increased activity was 17.2 minutes. In one of the four instances (25 per cent), there was an increase in blood pressure amounting to 16 mm. of mercury.

TABLE 4.—*Hartmann's Solution; Closed Abdomen Experiments*

	Total Observations	Normal Intestine	24 Hour Obstruction	48 Hour Obstruction	72 Hour Obstruction
Number of observations	20	7	7	2	4
Average dose per Kg. of body weight, cc.	1.16	1.1	1.4	0.9	0.98
Average blood chloride before, mg. per 100 cc.	547.6	564.2	539.8	712.5	672.7
Average blood chloride after, mg. per 100 cc.	670.7	632	645	730	745
Increase in blood chloride, per cent	16.3	12.2	19.8	3.9	10.8
Increased intestinal activity, per cent	95	87.5	100	100	100
No change in intestinal activity, per cent	5	12.5	0	0	0
Decreased intestinal activity	0	0	0	0	0
Average increase in tone, mm	20	25.6	16.2	28	13.5
Average increase in amplitude, mm	3.6	3	1.7	8.5	5
Average duration of increased activity, minutes	20.2	20.4++	17.2+	16.5	28.2

In two (50 per cent), there was no change in blood pressure and in one (25 per cent), the carotid cannula became clotted, so that the determinations could not be made (table 5, fig. 14).

SODIUM CHLORIDE, 20 PER CENT; CALCIUM CHLORIDE, 0.5 PER CENT

Five observations were made concerning the effect of the intravenous injection of sodium chloride, 20 per cent, and calcium chloride, 0.5 per cent, on obstructed intestine. Three of these were made on animals with forty-eight hour obstructions and two on those with seventy-two hour obstructions. The amount injected varied from 1.58 to 3.7 cc., the average being 2.2 cc. per kilogram of body weight. The blood chloride values before and after the administration of the hypertonic salt solution were 641.5 and 788.5 mg., respectively, an average percentage increase of 22.6. In each of the five instances, there was an increase in intestinal activity with increases in tone and amplitude of 73.8 and 16.6 mm., respectively. The average duration of this increased activity was 19.2 minutes (fig. 16). In the animals with

forty-eight hour obstruction, the average dose per kilogram of body weight was 1.5 cc. Blood chloride values in this group before and after the intravenous administration of the hypertonic salt solution were 641.5 and 788.5 mg., respectively, an average percentage increase of

Fig. 15.—Kymographic tracing showing the effect on seventy-two hour obstructed intestine of the intravenous administration of a hypertonic Hartmann's solution. There were periodic increases of intestinal tone and amplitude of intestinal movement. Associated with each increase in tone and amplitude, the animal apparently experienced pain as evidenced by crying (closed abdomen technic).

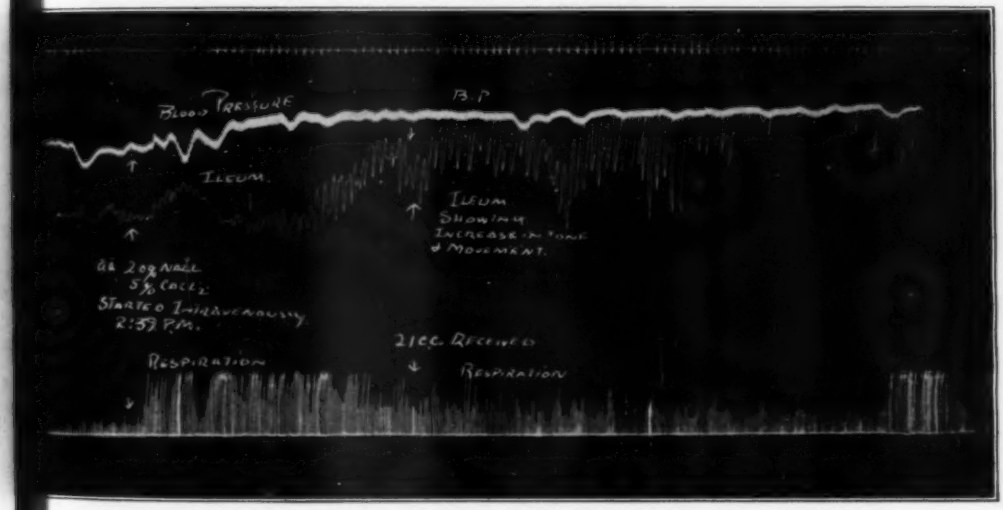

Fig. 16.—Kymographic tracing showing the effect on forty-eight hour obstructed intestine of the intravenous administration of sodium chloride, 20 per cent, and calcium chloride, 5 per cent. There was an increase in intestinal tone but more marked was the increase in the amplitude of intestinal movement. Approximately four minutes after the completion of the infusion, the intestine became more or less spastic (open abdomen technic).

22.6. In all instances (100 per cent) there were increases in intestinal activity, the increases in tone and amplitude being 74.6 and 14 mm..

respectively (fig. 18). The average duration of the increased activity was nineteen minutes. In the two observations made on animals with seventy-two hour obstruction, the average dose per kilogram of body weight was 3.3 cc. The average increases in intestinal tone and amplitude were 72.5 and 20 mm., respectively (fig. 19). The average duration of the increased activity was 19.5 minutes. The intravenous administration of sodium chloride, 20 per cent, and calcium chloride, 0.5 per cent, produced an average increase in blood pressure of 11 mm. of mercury in two instances (40 per cent), whereas in three (60 per cent), there was no change in blood pressure (table 5).

TABLE 5.—*Combinations of Sodium, Calcium and Potassium Chloride*

	Sodium Chloride, 20% Calcium Chloride, 0.5%			Sodium Chloride, 20% Calcium Chloride, 5%			Sodium Chloride, 20% Potassium Chloride, 0.5%		
	Total Observation	48 Hr. Obstruction	72 Hr. Obstruction	Total Observation	48 Hr. Obstruction	72 Hr. Obstruction	Total Observation	48 Hr. Obstruction	72 Hr. Obstruction
Number of observations	5	3	2	4	..	..	6	3	3
Average dose per Kg. of body weight, cc.	2.2	1.5	3.3	2.7	2.7	..	3.6	3.5	4.1
Average blood chloride before, mg. per 100 cc.	641.5	641.5	..	616.2	616.2	...	619.1	659	578.3
Average blood chloride after, mg. per 100 cc.	788.5	788.5	..	816	816	..	793.6	802.3	785
Increase in blood chloride, per cent	22.6	22.6	..	32.5	32.5	..	21.1	21.6	35.8
Increased intestinal activity, per cent	100	100	100	100	100	..	83.3	100	66
No change in intestinal activity, per cent	0	0	0	0	0	..	16.6	0	33
Decreased intestinal activity	0	0	0	0	0	..	0	0	0
Average increase in tone, mm.	73.8	74.6	72.5	25.7	25.7	..	58.8	78.6	20
Average increase in amplitude, mm.	16.6	14	20	12.5	12.5	..	19.4	26.6	8.5
Average duration of increased activity, min.	19.2	19	19	17.2	17.2	..	19.4	17	23

SODIUM CHLORIDE, 20 PER CENT; POTASSIUM CHLORIDE, 0.5 PER CENT

The effect of the intravenous administration of sodium chloride, 20 per cent, and potassium chloride, 0.5 per cent, on animals with forty-eight hour and seventy-two hour intestinal obstruction was determined in six instances. The amounts injected varied from 1.5 to 10.3 cc. with an average of 3.6 cc. per kilogram of body weight. The average blood chloride values before and after the administration of the hypertonic salt solution were 619.1 and 793.6 mg., respectively, an average percentage increase of 21.1. In all but one of the six instances (83.3 per cent) there were increases in intestinal activity. In the five in which there was an increased intestinal activity, the average increase in intestinal tone and amplitude were 58.8 and 19.4 mm., respectively.

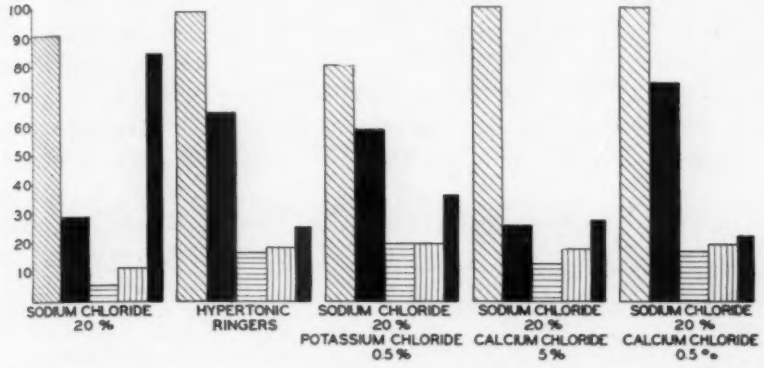

Fig. 17.—Graphic representation comparing the effects on intestinal activity of the intravenous administration of sodium chloride, 20 per cent, of a hypertonic Ringer's solution, of sodium chloride, 20 per cent, and potassium chloride, 0.5 per cent, of sodium chloride, 20 per cent, and calcium chloride, 5 per cent, and of sodium chloride, 20 per cent, and calcium chloride, 0.5 per cent. The hypertonic Ringer's solution produced a more marked increase in intestinal activity as regards increases in tone and amplitude and duration of activity than did sodium chloride, 20 per cent. Sodium chloride, 20 per cent, and calcium chloride, 0.5 per cent, was more efficacious in stimulating intestinal activity than sodium chloride, 20 per cent, and calcium chloride, 5 per cent, and also sodium chloride, 20 per cent, and potassium chloride, 0.5 per cent. The addition of potassium and calcium to sodium chloride increased the stimulating properties of the sodium chloride.

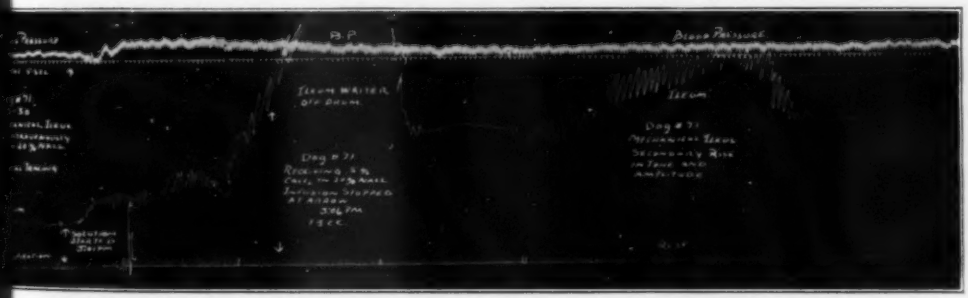

Fig. 18.—Kymographic tracing showing the effect on forty-eight hour obstructed intestine of the intravenous administration of sodium chloride, 20 per cent, and calcium chloride, 0.5 per cent. Almost immediately after the beginning of the infusion, there was a slight rise in intestinal tone associated with an increase in intestinal movement. After approximately one and one-half minutes, there was a sudden rise in intestinal tone which was so great that the writing lever passed off the kymographic drum. This was followed by an increased tone with a little movement, following which there was another period of increased activity consisting of an increase in intestinal tone and amplitude of intestinal movement (open abdomen technic).

The average duration of the increased activity was 19.4 minutes (figs. 17 and 20). In three animals with forty-eight hour obstruction, the average dose per kilogram of body weight was 3.5 cc. The average blood chloride values before and after the administration of the hypertonic salt solution were 659 and 802.3 mg., respectively, a percentage increase of 21.6. All of this group (100 per cent) showed increases

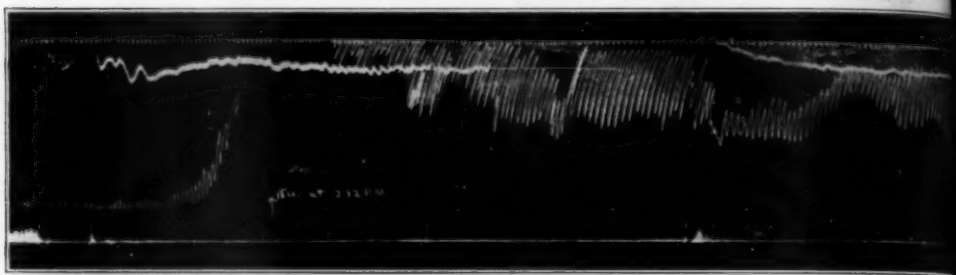

Fig. 19.—Kymographic tracing showing the effect on seventy-two hour obstructed intestine of the intravenous administration of sodium chloride, 20 per cent, and calcium chloride, 0.5 per cent. There was a sudden rise in intestinal tone associated with a very marked increase in intestinal movement. This persisted for a relatively long period of time (open abdomen technic).

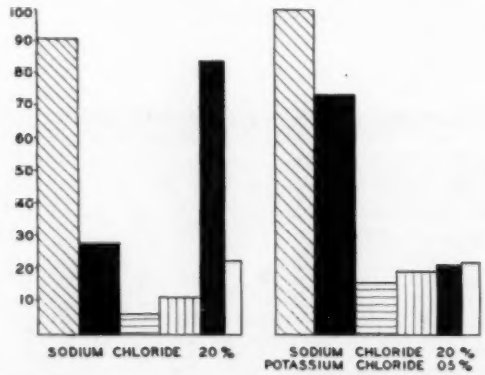

Fig. 20.—Comparison of the effect on intestinal activity of the intravenous administration of sodium chloride, 20 per cent, and potassium chloride, 0.5 per cent. There was a greater percentage of increase in intestinal activity following the administration of the latter solution than following the administration of the former. The increases in intestinal tone and amplitude of intestinal movement were also greater.

in intestinal activity with an average increase in tone and amplitude of 78.6 and 26.6 mm., respectively (fig. 21). The average duration of the increased activity was seventeen minutes. In the three animals with seventy-two hour obstruction, the average amount injected per kilogram

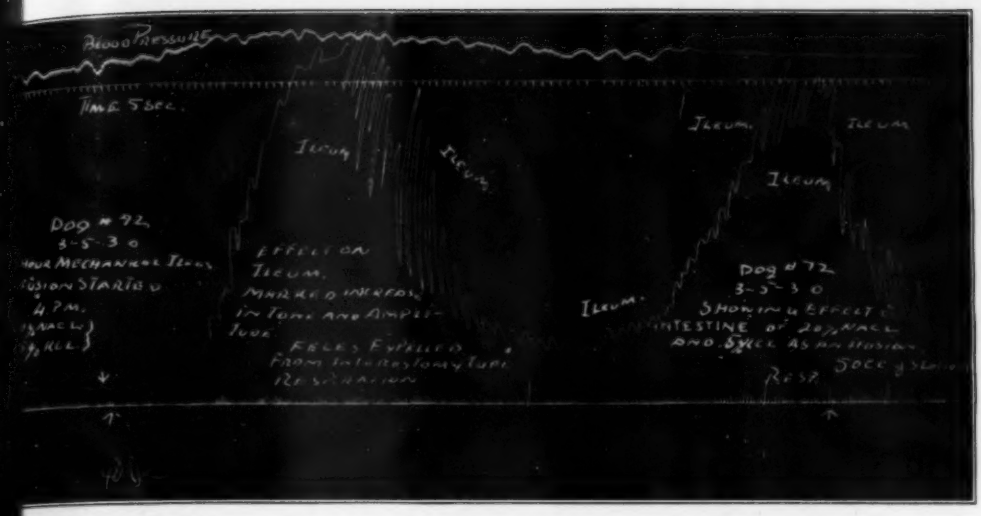

Fig. 21.—Kymographic tracing showing the effect on forty-eight hour obstructed intestine of the venous administration of sodium chloride, 20 per cent, and potassium chloride, 0.5 per cent. re occurred a marked increase in intestinal activity as evidenced by periodic increases in intes- tone and amplitude of intestinal movement (open abdomen technic).

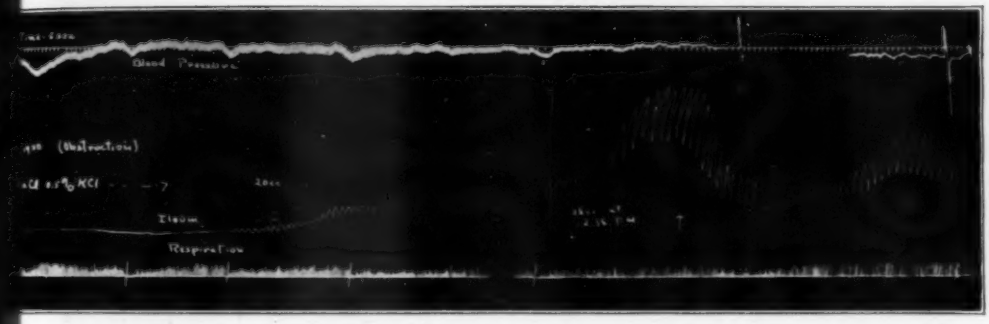

Fig. 22.—Kymographic tracing showing the effect on seventy-two hour obstructed intestine of intravenous administration of sodium chloride, 20 per cent, and potassium chloride, 0.5 per cent. re occurred first an increase in intestinal movement associated with a relatively slight rise in stinal tone. This, however, was followed by periodic increases in intestinal tone and amplitude en abdomen technic).

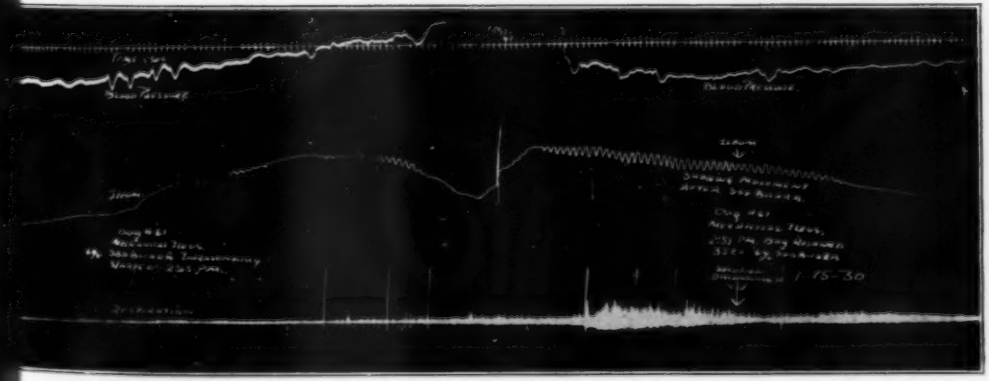

Fig. 23.—Kymographic tracing showing the effect on forty-eight hour obstruction of the intra- ous administration of sodium bicarbonate, 6 per cent. Almost immediately after the beginning of infusion, there was an increase in intestinal activity as evidenced by a rise in intestinal tone and an increase in the amplitude of intestinal movement (open abdomen technic).

of body weight was 4.1 cc. The average blood chloride values before and after the intravenous administration were 578.3 and 785 mg., respectively, a percentage increase of 35.8. Only two (66 per cent) of these three showed an increased intestinal activity, whereas one (33 per cent) showed no change in the activity. In the two in which there was an increase in intestinal activity, the average increases in tone and amplitude were 29 and 8.5 mm., respectively (fig. 22). The average duration of the increased activity was twenty-three minutes. In only five of the six instances in which sodium chloride, 20 per cent, and potassium chloride, 0.5 per cent, were used were blood pressure determinations made. In two (40 per cent), there was an average increase in blood pressure of 9 mm. of mercury. In two (40 per cent), there was no change in blood pressure, whereas in one, the carotid cannula clotted, so that the blood pressure could not be determined (table 5).

COMMENT

The advisability of administering chloride solutions to subjects with intestinal obstruction is now well appreciated, largely due to the investigations of Haden and Orr,[11] who showed that in high intestinal obstruction, at least, there almost invariably occurs a hypochloremia and an associated alkalosis. Raine and Perry[12] demonstrated that if a low intestinal obstruction persists long enough, a hypochloremia will also develop as in high obstructions. Clinically, chlorides have been administered largely in the form of physiologic or slightly hypertonic (1, 2 or 3 per cent) sodium chloride solutions, primarily for the purpose of combating the existing hypochloremia. Contrary to the negative results obtained by Hughson and Scarff[1] and Orr[4] with a physiologic sodium chloride solution, we have obtained an increased intestinal activity in 50 per cent of our observations made following the intravenous injection of a physiologic Ringer's solution (fig. 11). This reaction was, however, much less marked than that seen following the use of hypertonic solutions.

As a result of the original observations of Hughson and Scarff[1] and the investigations of Ross,[2a] the use of hypertonic sodium chloride solutions in the cases of adynamic ileus has become quite popular and

11. Haden, R. L., and Orr, T. G.: Chemical Changes in Blood After Intestinal Obstruction, J. Exper. Med. **27**:365, 1923; Effect of Sodium Chloride on Chemical Changes in Blood of Dog After Pyloric and Intestinal Obstruction, ibid. **38**:55, 1923; Effect of Inorganic Salts on Chemical Changes in Blood of Dog After Obstruction of Duodenum, ibid. **39**:321, 1924; Experimental High Intestinal Obstruction in the Monkey, ibid. **41**:107, 1925; Obstruction of the Jejunum: Effect of Sodium Chloride on Chemical Changes in Blood of Dog, Arch. Surg. **11**:859 (Dec.) 1925.

12. Raine, F., and Perry, M. C.: Intestinal Obstruction: Experimental Studies on Toxicity, Intra-Intestinal Pressure and Chloride Therapy, Arch. Surg. **19**:478 (Sept.) 1929.

in many instances life-saving. The exact mechanism by which hypertonic salt solutions stimulate intestinal activity is not known. Hughson and Scarff [1] showed that resection of the splanchnic and vagus nerves caused no alteration in the response of the intestine to hypertonic sodium chloride solutions. They also obtained no change in the response following the painting of a loop of intestine with 5 per cent procaine hydrochloride or 1:1,000 nicotine solution. A characteristic response was not obtained only when the blood supply to the loop of intestine was markedly interfered with. Bouisset and Fabre,[13] as a result of their experimentation, concluded that hypertonic salt solutions, by inhibiting the splanchnic effect, remove the inhibition exerted on the intestine by the splanchnics. They found the characteristic inhibition of intestinal activity following splanchnic stimulation could be prevented by the intravenous administration of hypertonic salt solution.

Dehydration of the organism resulting from the injection of the hypertonic solution cannot be the cause of the reaction, because we [14] have shown that the intravenous administration of a hypertonic dextrose solution invariably inhibits rather than stimulates intestinal activity. Hammett,[15] working with an isolated duodenal segment of the albino rat, found that the addition of sodium carbonate or sodium hydroxide to the surrounding fluid caused a contraction of the intestinal musculature. King and Church,[16] working with intact animals, found that the intravenous injection of sodium bicarbonate increased the intestinal activity. Dreyer and Tsung [2] found that an increased intestinal activity occurred following the intravenous injection of hypertonic solutions of sodium chloride, sodium sulphate, sodium bicarbonate and sodium carbonate. We have also been able to corroborate the finding that the intravenous injection of a hypertonic sodium bicarbonate solution caused an increase in intestinal activity (fig. 23). Hammett [16] expressed the belief that increased intestinal activity is the result of an increase in the hydroxyl ions and that relaxation occurs whenever there is an excess of hydrogen ions. King and Church [16] are also of this opinion. That the reaction is not due to the disturbance in the sodium-calcium balance is indicated by King and Church's results, in which they were unable to influence the reactions produced by the injection of sodium

13. Bouisset, L., and Fabre, P.: Action of Hypertonic Sodium Chloride on Extrinsic Innervation: Effects on Sympathetic, Compt. rend. Soc. de biol. **107:** 688, 1931.

14. Ochsner, Alton; Gage, I. M., and Cutting, R. A.: Effect of Insulin and Glucose on Normal and Obstructed Intestine, Proc. Soc. Exper. Biol. & Med. **29:**264, 1931.

15. Hammett, F. S.: Rôle of Change in Hydrogen-Ion Concentration in Motor Activity of Small Intestine, Am. J. Physiol. **60:**52, 1922.

16. King, C. E., and Church, J. G.: Motor Reaction of Muscularis Mucosae to Some Drugs, Am. J. Physiol. **66:**428, 1923.

bicarbonate by injecting soluble calcium salts. It is difficult to interpret the results which we have obtained following the intravenous injection of hypertonic salt solutions in view of the findings of these investigators, because even though the determination of the carbon dioxide-combining power of the plasma was not made, it is probable that in some of the animals, at least, there existed some degree of alkalosis. If such were present, the administration of hypertonic salt solution should, according to Hammett's and to King and Church's investigations, by decreasing the hydroxyl ions, actually produce a decrease in intestinal movement.

The present study confirms the previous experimental and clinical investigations as regards the stimulating effects of 20 per cent sodium chloride on obstructed bowel. We believe that we have also demonstrated, at least on the experimental animal with obstruction, that the use of hypertonic solutions containing other salts besides sodium chloride are more efficacious than the use of sodium chloride solutions alone. In considering our results, it is probably necessary to differentiate the results obtained in the experiments in which the open abdomen technic was used from those obtained in experiments in which the closed abdomen technic was used. The hypertonic Ringer's solution was used both in open abdomen and in closed abdomen experiments. The results obtained are not exactly comparable because the amounts of solution used in the open abdomen experiments (average 2.5 cc. per kilogram of body weight) were more than twice as large as the amounts employed in the closed abdomen experiments (average 1.17 cc. per kilogram of body weight). However, the response of the intestine to the intravenous injection of hypertonic salt solutions with the former was so much greater than with the latter that one is probably justified in assuming that the more marked results obtained with the former are at least in part due to the type of technic employed. There was an increased intestinal activity following the intravenous injection of the hypertonic Ringer's solution in 97.3 per cent of the open abdomen experiments and in 94.7 per cent of the closed abdomen experiments, which difference we believe can be disregarded. However, the average increases in tone in the open abdomen and the closed abdomen experiments were 61.2 and 16.1 mm., respectively. The increases in amplitude were 18.4 and 2.9 mm., respectively. The duration of this increased activity (17.6 minutes) was the same in both experiments. Even though larger amounts of the hypertonic Ringer's solution were used in the open abdomen experiments, the average percentage increase in blood chlorides was 22.5 as compared with 23.7 in the closed abdomen experiments. This was because the average normal blood chlorides before the intravenous administration of the hypertonic Ringer's solution was less in the closed abdomen experiments than in the open abdomen experiments. It is, therefore, obvious that a comparison of the results obtained

following the intravenous administration of hypertonic salt solutions should be made only when the same type of experiment is employed. Comparing the results obtained following the intravenous administration of 20 per cent sodium chloride solution in the animals with forty-eight and seventy-two hour obstruction with those obtained following the intravenous administration of the hypertonic Ringer's solution, both experiments being performed according to the open abdomen technic, considerable difference is noted (fig. 2). In spite of a much larger dose in the former instance (an average of 8.4 cc. per kilogram of body weight as compared with 2.5 cc. in the latter), in only 90.4 per cent was there an increase in intestinal activity as compared with 97.3 per cent when the hypertonic Ringer's solution was employed. In 4.4 per cent of the former group, there was no change in intestinal activity and in 4.4 per cent, there was an actual decrease. More significant are the changes in the tone and amplitude. The increases in tone obtained by the intravenous administration of the hypertonic sodium chloride solution and the hypertonic Ringer's solution were 28.6 and 61.2 mm., respectively. The average increases in amplitude were 5.05 and 18.4 mm., respectively. The average durations of the increased activities were 11.1 and 17.5 minutes, respectively. It is thus evident from these observations that the intravenous administration of a hypertonic Ringer's solution is more efficacious (even though much smaller doses are employed) in stimulating the intestinal musculature in the presence of obstruction than is a hypertonic sodium chloride solution.

By comparing the results obtained following the intravenous administration of a hypertonic Ringer's solution with those obtained following the intravenous administration of a Hartmann's "hypertonic" combined solution (the closed abdomen technic was used in both), the following was noted (fig. 7): In both experiments the dose was practically the same (1.17 cc. of Ringer's solution and 1.16 cc. per kilogram of body weight of Hartmann's solution). In both groups, there were approximately the same percentage increases in intestinal activity. However, there was some difference in the character of the response of the intestine to the intravenous administration to the hypertonic solutions. The average increases in tone following the administration of hypertonic Hartmann's solution and Ringer's solution were 20 and 13.1 mm., respectively, whereas the increases in amplitude were 3.6 and 2.9 mm., respectively. The durations of the increased activities were 20.2 and 17.6 minutes, respectively. One would expect little difference in reaction of the intestine to these two hypertonic solutions because of their similarity. The hypertonic Ringer's solution as employed contains 18 per cent sodium chloride as compared with 11.7 per cent in the hypertonic Hartmann's solution. Sodium lactate, 5.6 per cent, is contained in the hypertonic Hartmann's solution but not in the hypertonic Ringer's

solution. Potassium chloride contents in the hypertonic Ringer's and the Hartmann's solution are 0.6 and 0.7 per cent, respectively. The calcium chloride contents were practically the same, 0.52 per cent in the hypertonic Ringer's solution and 0.54 per cent in the hypertonic Hartmann's solution. The principal differences are that there is a higher concentration of sodium chloride in the hypertonic Ringer's solution, and the hypertonic Hartmann's solution contains sodium lactate.

It is apparent that the administration of other salts besides sodium chloride is of value in stimulating the intestine. Whitehead [17] found, working with ileal and jejunal segments employing the Magnus technic, that the addition of calcium and potassium to the solution in amounts exceeding isotonicity caused a progressive increase in tone and a decrease in amplitude. In our intact animal experiments, we found not only a much more marked increase in tone in the animals receiving the hypertonic Ringer's solution, but also a materially increased amplitude. The duration of the increased activity was greater in the animals receiving the hypertonic Ringer's solution.

The relative effects of the addition of calcium and of potassium to sodium chloride solutions were also determined in the present investigation. However, the number of observations made following the intravenous administration of each is so small that few or no positive deductions can be made. Tht effect of sodium chloride, 20 per cent, and calcium chloride, 5 per cent, in forty-eight hour obstructed intestine was determined in four instances. In all instances, there was an increase in intestinal activity. Similar results were obtained by the intravenous administration of sodium chloride, 20 per cent, and calcium chloride, 0.5 per cent. In five observations, the character of the reaction obtained was much more marked than that obtained with a higher concentration of calcium chloride. The average increase in tone following the intravenous administration of sodium chloride, 20 per cent, and calcium chloride, 5 per cent, was 25.7 mm. as compared with 73.8 mm. increase in tone from the intravenous injection of sodium chloride, 20 per cent, and calcium chloride, 0.5 per cent. The average increases in amplitude were 12.5 and 16.6 mm., respectively. The average durations of the increased activities were 17.2 and 19.2 minutes, respectively. That the addition of calcium chloride to a hypertonic sodium chloride solution enhances the value of the solution as an intestinal stimulant is evidenced by the difference in the results obtained by sodium chloride, 20 per cent, alone and sodium chloride, 20 per cent, combined with calcium chloride, 0.5 per cent (fig. 17). This difference was especially marked in the animals with forty-eight hour obstructions. Intestinal activity was increased 94.1 per cent. It was increased 100 per cent in

17. Whitehead, R. W.: Responses of Excised Intestines to Alterations of Electrotype Concentrations (Na, Ca, K), Am. J. Physiol. **89**:253, 1929.

the animals with forty-eight hour obstruction receiving sodium chloride, 20 per cent, and sodium chloride, 20 per cent, combined with calcium chloride, 0.5 per cent, respectively. The average increases in tone were 20.5 and 74.6 mm., respectively, and the average increases in amplitude were 2.25 and 14 mm., respectively. The average duration of the increased activities were five and nineteen minutes, respectively. A comparison of the results obtained by the two hypertonic solutions is not free from criticism, because even though in each the open abdomen technic was used, the number of observations is not the same. Twenty-one observations were made with sodium chloride, 20 per cent, whereas only five were made with sodium chloride, 20 per cent, and calcium chloride, 0.5 per cent. Whitehead [17] found that the addition of calcium alone to the perfusing fluid in his investigations with ileal and jejunal muscle strips caused an increase in rate and tone and a decrease in amplitude as the concentration of calcium was increased above isotonicity. We found also an increase in amplitude as well as an increase in tone, but little change in rate (figs. 18 and 19). Whitehead [17] also observed that periodicity occurred when calcium was added to the solution, which was also evident in our experiments (fig. 18). The addition of calcium chloride, 0.5 per cent, to the sodium chloride, 20 per cent, had a more markedly stimulating effect on the intestine than the addition of calcium chloride, 5 per cent. It is possible that the excessive amounts of calcium chloride present in the 5 per cent solution may have exerted an inhibitory effect on the musculature of the intestine, as suggested by the investigations of Kennedy,[18] Bauer, Salter and Aub,[19] and Alvarez.[20] In subsequent experiments, Fitzhugh, Miller, Taylor and Aub [21] were unable to show experimentally that calcium, even in high concentrations, decreased the intestinal activity.

Rather interesting results were obtained following the intravenous administration of sodium chloride, 20 per cent, and potassium chloride, 0.5 per cent. The dose employed was relatively large, 4.6 cc. per kilogram of body weight as compared with 2.2 cc. in the group receiving sodium chloride, 20 per cent, and calcium chloride, 0.5 per cent. There was considerable difference in the response to the two solutions.

18. Kennedy, W. P.: Normal Response of the Isolated Uterus and the Response After Experimental Interference, Quart. J. Exper. Physiol. **16**:332, 1927.

19. Bauer, Walter; Salter W. T., and Aub, J. C.: Studies of Calcium and Phosphorus Metabolism, Xa: The Use of Calcium Chloride to Relieve Peristaltic Pain, J. A. M. A. **96**:1216 (April 11) 1931.

20. Alvarez, W. C.: Influence of Drugs on Intestinal Rhythmicity, Am. J. Physiol. **46**:554, 1918.

21. Fitzhugh, Greene; Miller, M. L.; Taylor, G. W., and Aub, J. C.: Studies of Calcium and Phosphorus Metabolism, Xb: The Effect of Intravenous Calcium Chloride on Peristalsis Following Intestinal Obstruction in Dogs, Am. J. Physiol. **97**:142, 1931.

Whereas in the group receiving the solution containing calcium chloride there was stimulation in the intestine in all (100 per cent), in the group receiving the solution containing potassium chloride, there was stimulation of the intestine in only 83.3 per cent. The increases in tone in the groups receiving calcium chloride and potassium chloride were 73.8 and 59.8 mm., respectively. The increases in amplitude were 16.6 and 19.4 mm., respectively. The durations of these increased activities were 19.2 and 19.4 minutes, respectively. It is thus apparent, if one is justified in comparing the results obtained in the relatively small group of experiments in which potassium was added to the sodium chloride, that the addition of potassium to the hypertonic sodium chloride solution is efficacious in stimulating the intestine. Whitehead [17] found following the removal of potassium from the perfusion fluid in the Magnus preparation that the restoration of the potassium always resulted in a characteristic temporary inhibition of the activity of the intestinal musculature. However, the addition of potassium above normal resulted in a progressive rise in tonus and a characteristic periodicity, which was also evident in our experiments (fig. 21). Alvarez [20] also showed that the addition of potassium salts increased the tone and amplitude of intestinal movement. It is apparent from our investigations that in the experimental animal, at least, the administration of calcium and potassium to sodium chloride is of advantage in stimulating the intestine in the presence of obstruction, as the intravenous injection of the hypertonic Ringer's and hypertonic Hartmann's solutions were more efficacious than the intravenous injection of the hypertonic sodium chloride solution alone.

We have used the hypertonic Ringer's solution clinically with very gratifying results and feel, on the basis of our experimental observations and our clinical results, that its use is justified. In the clinic, we have employed from 10 to 15 cc. of the 20 per cent Ringer's solution or the Hartmann's solution prepared in the way described. It is extremely important that this solution be given slowly, not faster than 1 cc. per minute, in order to obviate any danger of sodium poisoning. Within a short time after the intravenous administration, a rectal tube should be introduced, and if no results are obtained, an enema should be given because frequently an emptying of the small bowel into the colon occurs without defecation. Probably the greatest danger from the use of hypertonic salt solution is the increased coagulability of the blood, which danger, however, can be obviated by using amounts not greater than 10 to 15 cc. and injecting the solution slowly. We have repeated the injection as often as every eight hours and feel that such a procedure is justified in those cases in which normal reestablishment of intestinal movement has not occurred.

PERINEAL PROSTATECTOMY

PRESENTATION OF THE WILDBOLZ TECHNIC

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LOS ANGELES

The controversy concerning the relative merits of the perineal and suprapubic routes of prostatectomy has finally become somewhat stabilized. Successful results in prostatectomy depend on the method in which the surgeon is trained and on variables of the individual case.

The method of suprapubic prostatectomy has been to a great extent standardized. However, the perineal route has not as yet reached full maturity, and in its growth has been wont to arouse the concern of many of its benefactors. The numerous approaches and modifications, many of which have been put forth by foreign contributors, have left many groping for the most proficient and efficacious route.

The medical profession owes much to Young and his pioneer work in standardizing a perineal route, and to the work subsequently carried on by his pupils. However, in order to establish a final clarity, the various methods should be put forth and clearly stated.

The methods of perineal approach may be briefly summarized as:

I. Median transurethral methods
   1. Berndt
   2. Praetorius
   3. Alexander
   4. Syms
   5. Goodfellow

II. Ischiorectal method of Voelcker

III. Wilm's lateral approach

IV. Anatomic conservation by surgical dissection of perineum
   1. Zuckerkandl
   2. Proust
   3. Young's operation and modifications
      (*a*) Geraghty
      (*b*) Transprostatic en masse enucleation
      (*c*) Complete extracapsular prostatoseminal vesiculectomy for cases of pure hyperplasia with pronounced infection and vesiculitis
   4. The Wildbolz method

From the Chirurgische Klink am Inselspital, Berne, Switzerland.

While working with Professor Voelcker at Halle, Germany, I had the chance to help in performing and later to perform his ischiorectal prostatectomy. In other European clinics, namely, in Berlin with Prof. A. von Lichtenberg at the St. Hedwig's Krankenhaus, and in Berne, Switzerland with Prof. Hans Wildbolz at the Chirurgische Klinik am Inselspital, other methods of perineal prostatectomy were used which afforded me the opportunity to make a comparative study of the various methods.

With the cooperation of Professor Wildbolz, I have the opportunity to present to American literature the illustrated technic of the Wildbolz method of perineal prostatectomy. Possessing a working acquaintance with the Young method and its modifications, as well as the German methods of Voelcker, Wilms, Zuckerkandl and others, I am presenting this paper as a comparative study to clarify the various methods of perineal approach, as well as to present the Wildbolz method.

In the various methods of perineal prostatectomy used in America, the most conspicuous disadvantage is the possible occurrence of postoperative incontinence. To some surgeons this factor always looms as an obstacle in adopting the perineal method as a routine. It became necessary, therefore, for some one to modify the technic so as to avoid this possibility. The Wildbolz method overcomes postoperative incontinence by not exposing, opening or disturbing the membraneous urethra and its musculature. Moreover, in that it is a purely intracapsular enucleation of the adenomas, both urinary sphincters are carefully preserved.

The entire urethral musculature, as emphasized by Schwarz, must be considered as a single functional unit. However, of the whole urethral unit, the external and internal sphincters are the most important. The reliability of urinary control is directly dependent on the intactness of the external sphincter. Further, in the mechanism of urinary control, the internal sphincter plays a lesser rôle than the external sphincter. However, the internal sphincter can at times act to produce a watertight exit, as exemplified in cystograms.

This was also observed clinically by Wildbolz in patients during the first days following perineal prostatectomy, when they were left without retention catheters. The bladder would arbitrarily empty itself through the perineal wound, but between micturitions, the wound, although lying in front of the internal sphincter, remained dry.

The events that occur during the normal ejaculation of semen show how completely the internal sphincter can control the urinary flow. During the act of ejaculation the external sphincter opens completely, and yet not a drop of urine flows out, thus showing that the

internal sphincter can withhold the urine in the bladder without the aid of the external sphincter.

As depicted, the internal sphincter is quite important, but hardly the main factor in urinary control as many have tried to maintain. If this were true, some bladder incontinence should more frequently occur following suprapubic prostatectomy in which the internal sphincter is frequently greatly dilated, at times even torn. These facts were also borne out by Illyés, who noted by urethroscopic examination, following suprapubic prostatectomy, that a functional loss of the internal sphincter occurred.

Other evidence to verify the lesser importance of the internal sphincter as compared to the external sphincter is presented by the catheter test of Finger and Wildbolz; namely, that a catheter passed just beyond the external sphincter into the posterior urethra will drain the contents of the bladder without any strangury, but as soon as the catheter is pulled distal to the external sphincter, the urinary flow will cease.

It becomes obvious that the internal sphincter should by all means be protected during prostatectomy, but, even more important, it is necessary to maintain an intact external sphincter so as to have a watertight control of the bladder following the procedure. It is the preservation of the external sphincter which is not given sufficient attention in most of the present day methods of perineal prostatectomy.

In the method of Albarran and Proust, which was the first most commonly used, the prostatic capsule was split in its entire length from the membraneous portion of the urethra to the neck of the bladder, and on account of this the external sphincter was necessarily injured. The instruction of Young to insert the retractor through the membraneous portion of the urethra also led unavoidably to an injury of the external sphincter. This is further exemplified in the recommendation of Berndt and Praetorius to split the external sphincter as a routine in their method, the so-called median perineal prostatectomy. It is obvious that by such procedure, urinary control would be frequently made uncertain. Even Zuckerkandl, with whom Wildbolz most nearly agrees, did not attach sufficient importance to the external sphincter, in that he split the prostatic capsule too far distally. He began the capsular incision at the root of the membraneous portion of the urethra and carried it very far proximally onto the prostatic capsule. Zuckerkandl realized that this constituted a weak spot in his method, as was brought out by the following words: "By this method one succeeds in isolating the urethra to a greater extent than is possible by the Freyer operation, inasmuch as the cuticular portion is also loosened from its surroundings."

The main goal in developing the Wildbolz method of perineal prostatectomy is to preserve the external sphincter in its entire function in

spite of the complete enucleation of the prostate; therefore, any preparation or exposure of the membraneous urethra is avoided. It is planned to leave this portion of the urethra and its enveloping external sphincter completely undisturbed and uninjured and out of the field of operation. In order to accomplish this and to preserve all the muscular bundles of the external sphincter which encircle the prostatic portion, the capsular incision is placed as far as possible toward the bladder. The external sphincter is composed not only of encircling striated muscle enervated by the pudendic nerve, but also of smooth muscle enervated by the autonomic nerves. These muscle bundles extend on to the apex of the prostate. The Wildbolz prostatic capsular incision was therefore chosen to allow this important muscle ring and its extension on to the prostate to remain intact.

It is quite unimportant as to whether or not the ejaculatory ducts are patent following the operation, because the routine bilateral vasotomy, either before or at the time of operation, disturbs the patency of the seminal passages. Potency does not depend so much on the patency of the ejaculatory ducts as on the complete preservation of the nerves approaching the prostate gland.

Wildbolz stated:

> That the difference of incision between Zuckerkandl and myself is not unimportant as regards efficient urinary control is shown by the fact that Zuckerkandl has not used his method very often on account of the frequency of postoperative incontinence, and therefore, he usually prefers the supra-pubic method; whereas with my method, I have obtained such good results that for 20 years I have continued to use the perineal prostatectomy and consider it the method of choice. To him who doubts the good bladder control following my operation, I wish to give this thought, namely, that if my patients had an unsatisfactory urinary control following the operation, they would have influenced other prospective patients to avoid prostatectomy at my hands, and would have sought the help of other surgeons who use the supra-pubic method; because it is well known that a surgeon's failures become known more quickly amongst his colleagues and hospital circles than his successes.

TECHNIC

The operation is almost always carried out with sacral anesthesia. In less than 10 per cent of the cases in which local anesthesia does not work completely, or due to hyperanxiety of the patient, ether anesthesia is used. The patient is placed in an exaggerated lithotomy position, with the thighs sharply flexed against the abdomen, so that the perineum is completely exposed and tense. A metal catheter is passed by way of the urethra into the bladder and left in place.

The operation begins with the semicircular perineal incision of Zuckerkandl, which extends from one ischial tuberosity to the other, with the convexity toward the scrotum, about a thumb's thickness below the dorsal edge of the bulb. After splitting the subcutaneous fat and the superficial perineal fascia, one is able to discern the bulbous raphe in the middle of the wound by a light dorsal pull on the undersurface of the wound. With short sharp incisions made close to the

raphe of the bulb, the posterior end of the urethral bulb is dissected out. This is made easier by means of blunt dissection of the fatty tissue hanging on to the sides of the bulb, after which the bulb will clearly protrude into the wound. The lateral portions of the perineal incision should not be cut too deeply so as not to injure the branches of the pudendic nerve which supply the external sphincter. Following the dissection of the posterior bulbous end, the patient is frequently placed in a semi-Trendelenburg position. This is done so that during the following dissection around the posterior end of the bulb the light may be thrown into the depths of the wound, in order that the recto-urethral muscle extending posterior to the bulb may be clearly seen.

By pulling down the posterior edge of the wound with a flat retractor, or even better by means of the fingers, the rectum and recto-urethral muscle will be put on a stretch. In order to avoid any danger of a rectal injury, the recto-urethral muscle must be sharply divided near the urethral bulb (fig. 1). After this muscle is cut through, the rectum and levator ani will fall posteriorly, and the bulbous

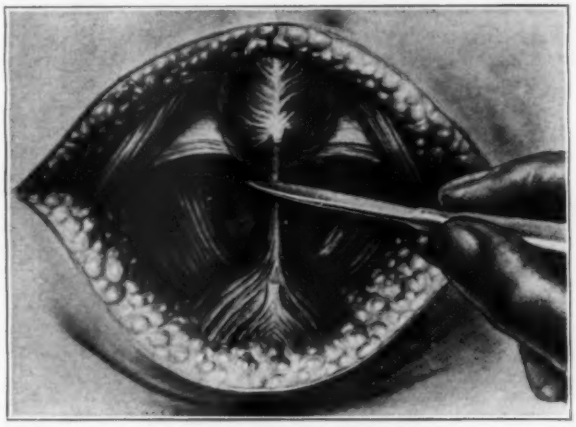

Fig. 1.—The perineal incision has been made, the muscles exposed, and the recto-urethral muscle is being severed near the urethral bulb. (The illustrations in this article are from the monograph of Hans Wildbolz: Technik der perinealen Prostatektomie, Urologische Chirurgie, Berlin, Julius Springer, 1929.)

urethra and superficial transverse perineal muscles will remain anteriorly. The approach to the posterior aspect of the prostate will now be free. When the metal catheter that has been lying in the urethra is grasped and the prostate pushed prominently into the wound, the posterior aspect of the prostate, even though not immediately visible, will be easily palpable. Thus a straight line of direction from the perineal wound direct onto the prostate may be followed. The connective tissue layer which will be found on the posterior aspect should not be split far to the front, but always toward the bladder. In this manner it is possible to make the posterior aspect of the prostatic capsule completely visible without the slightest injury. The capsule may be recognized by its shimmering whiteness and unusual tenseness. Before the capsule is split, an area no larger than the size of a quarter should be exposed, and great care should be taken not to expose the capsule to too great an extent from the fascia of Denonvieller. The exposed prostatic capsule is now split in the median line by a vertical incision.

Whether the capsule is split laterally or in a median line is apparently without great importance. The median incision is preferred because it gives equally good approach to both lateral lobes, and undoubtedly more effectively preserves the nerves that lead to the prostate both posteriorly and laterally. Of greater importance than the question of either a median or a lateral incision is the fact that the incison must begin sufficiently far beyond the external sphincter to leave the latter completely intact.

The incision into the prostatic capsule should begin as far as possible from the apex of the prostate toward the bladder, about 1.5 cm. superior to the inferior edge of the point where one begins to feel the prostatic adenoma (fig. 2). It should extend superiorly to the furrow between the prostate and seminal vesicles. The importance of commencing the capsular incision as far as possible toward the bladder from the inferior edge of the adenoma is stressed, for then the muscle ring that surrounds the membranous portion of the urethra remains intact, and

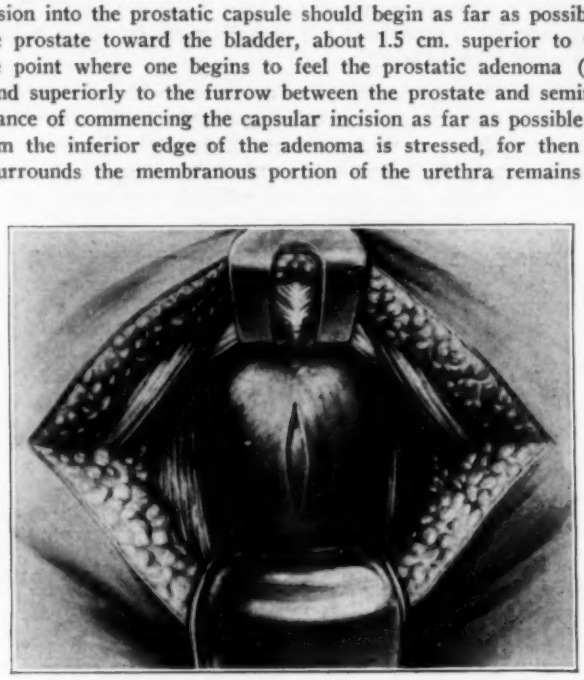

Fig. 2.—With retractors in place, the prostate and its capsule are in sight. The latter is split vertically close to the bladder.

the smooth muscle bundles of the sphincter that envelop the distal portion of the prostatic urethra are also preserved. The incision into the prostatic capsule should extend so deep into the adenoma that when the wound is separated the dividing line between the prostatic capsule and the adenoma is distinctly visible. It is not desirable at this point to cause an opening into the urethra with the initial capsular incision; however, it is not always preventable when the posterior commissure of the adenoma is very thin.

A Kocher gland enucleator is now inserted in the cleavage line between the adenoma and the prostatic capsule. As soon as a small opening is created between the capsule and the adenoma, one proceeds to enucleate the adenoma subcapsularly by means of the forefinger. During the enucleation, special care must be taken to loosen the underportion of the adenoma from the prostatic urethra as well as from the base of the bladder, so as to avoid urethral tears in either place.

After the adenoma is loosened from the prostatic capsule both posteriorly and laterally, no further enucleation is carried on until the urethra is severed as close

to the inferior end of the adenoma as possible, in order to prevent any irregular tear into the urethra or any injury to the muscle fibers of the external sphincter. This is carried out in the following manner: The index finger of the left hand is placed between the prostatic capsule and the adenoma, and the latter is pushed as far as possible toward the bladder; at the same time the urethra around it is loosened as much as possible. With the volar surface of the index finger as a guide, the urethra is cut at this point (fig. 3).

This division of the urethra is ordinarily made proximal to the colliculus seminalis, as can be verified by urethroscopic examination. The adenomatous nodules of the prostate always develop around that portion of the urethra which lies between the colliculus and the bladder, and never peripheral to the colliculus. Thus the urethra is cut close to the lower pole of the adenoma so that the colliculus will always lie distal to it, and will be preserved. This has been proved by urethroscopy, as well as in cases that have gone to autopsy.

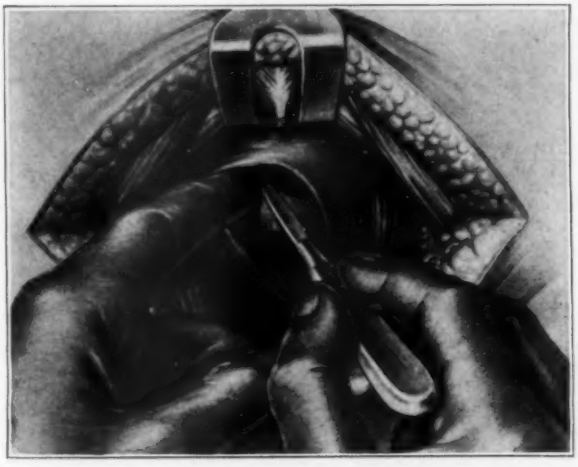

Fig. 3.—The adenoma has been loosened from the capsule and the former is pushed as far as possible toward the bladder. The urethra is severed immediately distal to the adenoma.

Following the division of the urethra at the lower pole of the prostatic adenoma, the distal portion of the prostatic urethra with the colliculus seminalis will retract anteriorly inside the prostatic capsule, and thereby escape the danger of any tears or injury which it might otherwise sustain during the following completion of the prostatic adenoma enucleation. The Young retractor is now easily inserted into the proximal portion of the urethra which is still surrounded by the prostatic adenoma. That portion of the prostate still attached to the floor of the bladder and seminal vesicles is now pulled forward into the wound and freed from the remaining attachments (fig. 4). In most cases, the adenoma will remain in one large mass, and only seldom will it fall apart into two or three nodules. After the enucleation of the prostate, a finger may be passed through the opening of the bladder which will feel like a ring, and as a rule the sphincter will contract down on the finger. It is difficult to preserve the entire intactness of the internal sphincter even by perineal prostatectomy when the adenoma has a large middle lobe which protrudes markedly into the bladder or has developed entirely intra-

vesically. During the enucleation of such a middle lobe, the internal sphincter is usually overstretched or even injured through tearing. However, only seldom is it so severely injured as to cause the opening of the neck of the bladder to gape.

With the index finger within the sphincter of the neck of the bladder as a guide, artery forceps are applied; one above, one below, one to the right and one to the left. With these four forceps, the sphincter and neck of the bladder are pulled forward into the wound, making it easier to examine the inside of the bladder with the index finger. Thus it may be definitely determined during the enucleation that no adenomatous nodules, particularly so-called middle lobe nodules, have been left at the exit of the bladder. After examining the inside of the bladder, it is thoroughly irrigated with physiologic solution of sodium chloride so as to prevent the formation of a blood clot which might later plug the retention catheter.

Following the thorough cleansing of the bladder, the opening is pulled into the wound by the four forceps, and the latter are replaced by four catgut sutures.

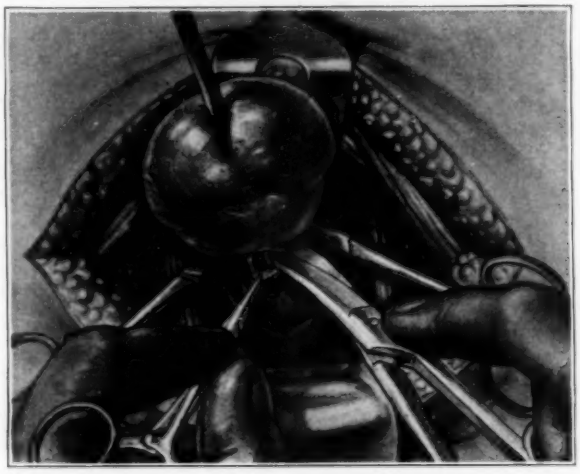

Fig. 4.—A Young retractor has been inserted into the bladder through the prostatic urethra surrounded by the adenoma, which is now pulled forward and removed by severing its remaining attachments with the bladder and seminal vesicles.

These sutures remain untied and are retained in place by clamping with forceps. So that the relation of these ligatures with the neck of the bladder may not be confused, they are fastened to the sheets, in their four respective quadrants. A metal catheter is now passed through the anterior urethra and through the operative area into the bladder. The catheter causes the distal stump of the urethra, which had retracted forward into the capsule after resection, to become clearly visible in the operative wound, and it may now easily be sutured to and with the opening of the neck of the bladder (fig. 5).

The metal catheter must be replaced by a no. 20 silk catheter before the ligatures between the neck of the bladder and the stump of the urethra are tied. Following the passage of the silk catheter, the ligatures are tied, joining the neck of the bladder and the urethra, while the catheter remains in place. The sutures joining the neck of the bladder and the urethral stump are usually sufficient to

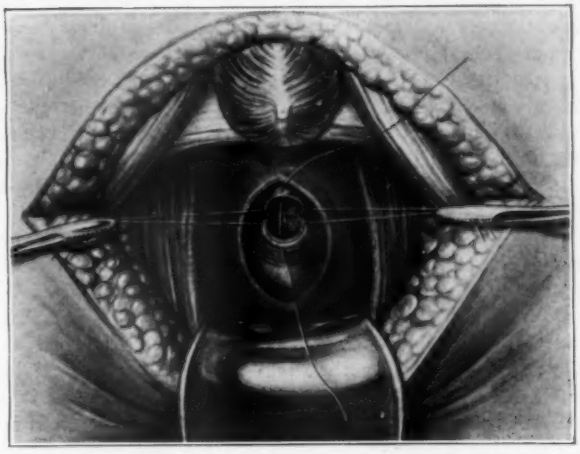

Fig. 5.—The distal and proximal ends of the urethra are united to carry out complete anatomic reconstruction.

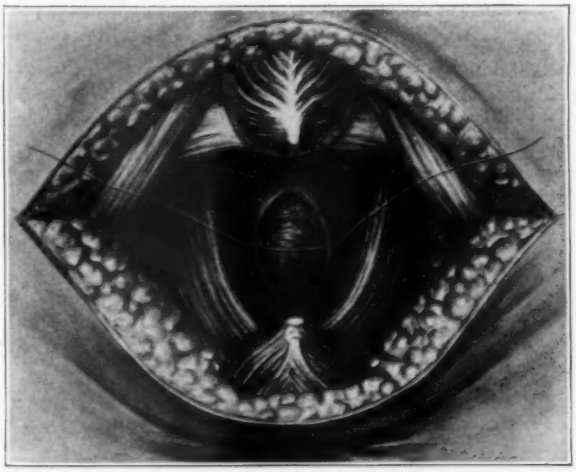

Fig. 6.—The edges of the prostatic capsule which had been split at the beginning of the operation are brought together and sutured, thus making the reconstruction complete.

control any bleeding from the edges of the urethra and bladder wounds. Only occasionally will additional sutures for hemostasis be necessary. Usually after the bladder-urethral sutures are tied, the wound will be entirely dry.

In order completely to reconstruct the anatomic relationships at the neck of the bladder, and above all to restore complete function of the muscular bundles extending on to the prostatic capsules from the external sphincter, the edges of the prostatic capsule which had been split at the beginning of the operation are now brought together and sutured (fig. 6). At this point of reconstruction, the edges are not always clearly visible in the wound, for during the enucleation of the adenoma they may have retracted laterally. They are, however, easily located, grasped with a forceps and pulled toward the middle of the wound. This lateral retraction of the prostatic capsule indicates the importance of bringing them together after the operation. Thus, by reconstruction of anatomic relationships to as nearly normal as possible, a rapid healing is promoted.

Prior to closing the perineal wound, it should be made certain that the anterior rectal wall has not been injured during the operation. A rectal examination is made and the anterior wall is pushed into the wound, so that injury, if it has occurred, can best be seen. Should the musculature be thinned in any place or the rectal mucosa injured in any way, it must be sutured and reinforced by a layer of levator ani muscle. However, where it is clear that the rectum has not been injured, such suture in the levator ani muscle is unnecessary.

Tamponage of the operative wound and drainage of the bladder through the perineal wound should not be done. Tamponage or drainage of the bladder unnecessarily delays healing of the wound by one to two weeks. To insure good drainage of any secretion, all that is necessary is the placing of a small cigaret drain into the wound extending down to, but not within, the prostatic capsule. The perineal wound should then be rather tightly closed, including skin and subcutaneous tissue, allowing only a small opening for the drain.

Prostatectomy should be immediately preceded or followed by a bilateral vasotomy, which practically always prevents a postoperative epididymitis. To undertake this vasotomy sometime before the prostatectomy in order to prevent an epididymitis during the preoperative retention catheter stage is disadvantageous. To most patients this minor procedure will appear as a major operation and will frighten them. Such a psychic strain may harm the debilitated patient almost as much as a possible epididymitis.

POSTOPERATIVE CARE

The perineal drain is removed three days after the operation, and the drainage canal is irrigated daily with hydrogen dioxide through a small catheter. The bladder is irrigated twice daily through the retention catheter with 1:2,000 oxyquinolin sulphate solution during the first three days and later with 1:5,000 oxycyanide solution.

On the third postoperative day the necessary measures to insure a bowel movement are given. From the fourth postoperative day on, the patient is allowed up daily for from two to three hours.

The retention catheter is left in place until the perineal wound is entirely closed, which usually takes from two to three weeks. A change of the retention catheter is usually unnecessary during this time; however, should it be necessary, it can easily be carried out with the help of a mandarin. It is not unusual for the perineal wound to remain entirely dry until the complete closure. There may be some drainage from the perineal wound, and it is most frequently observed between the sixth and twelfth postoperative days. Signs of inflammation in the perineal

wound hardly ever occur, even in cases in which the bladder had been infected preoperatively. Should inflammation occur, it can easily be controlled by the application of warm salicylate compresses.

COMMENT

Rapid healing and permanent reconstruction of the bladder function is obtained by this method. In the majority of cases the operative wound closes within two weeks, and in only the very exceptional case does closure take more than three weeks. The bladder control is practically always intact. Following the removal of the retention catheter, a few patients when coughing or sneezing have temporary postoperative weakness of the sphincter muscle. Almost without exception, these symptoms of incontinence disappear after a few days. It may be stated without fear of contradiction that with this method of perineal prostatectomy one need never fear permanent postoperative incontinence.

The Wildbolz method also excludes many disadvantages of other methods of perineal prostatectomy, namely, fistulas and postoperative hemorrhage. Perineal fistulas which formerly occurred in over 7 per cent of the cases of perineal prostatectomy as shown by the accumulated literature of Pousson, no longer occur by this method of perineal prostatectomy. The perineal wound closes quickly. The occurrence of urinary fistulas is frequently mentioned in the literature as a fairly common sequela of perineal prostatectomy. This can be explained only by the fact that frequently a perineal drain is left extending all the way into the bladder.

With the Wildbolz method this complication is prevented by completely anastomosing the bladder with the urethra and placing the perineal drain to, but not into, the prostatic capsule. Experience has shown that with this technic the danger of a recto-urethral fistula is relatively small, even though its occurrence is not impossible with any method of prostatectomy.

An open incision into the rectum when exposing the prostate can definitely be prevented. However, the danger of tearing the rectum by careless handling of the perineal wound retractors is to be constantly held in mind. In order to prevent this, only very light traction should be applied to the retractor which pulls the rectum away from the operative field. Pressure against the rectum with the tip of the retractor must be particularly avoided, and the assistants must be instructed always to hold the retractor with its full flat surface against the rectal wall. Even if an open tear into the rectal wall is avoided during the course of the operation, a rectal fistula may develop. Most of these patients suffer from arteriosclerosis, so that too great exposure of the anterior rectal wall may so disturb its blood supply that secondary necrosis of the wall may occur. However, it is rather improbable that

such a necrosis will occur without any operative injury, particularly where there is no pressure of the perineal drain. Such a secondary necrosis of the rectal wall, according to my experience, is always a result of operative injury of the rectal musculature. As previously stated, the rectal wall should be carefully examined at the termination of the operation, and if injury is found, it is to be properly repaired.

The dangers of perineal prostatectomy which were previously so greatly feared, namely, urinary incontinence, fistulas and postoperative hemorrhage, are almost entirely eliminated by this method. Owing to these experiences, perineal prostatectomy may be more commonly utilized, because in many respects this method offers certain superior advantages over the suprapubic method, the foremost one being that it causes much less operative shock. It is true that the operative shock of suprapubic prostatectomy has been greatly decreased through the use of the two-stage operation; nevertheless, it is still greater than in perineal prostatectomy. This can be seen by observing the patient immediately after operation. The patient who has undergone perineal prostatectomy is not especially ill following the procedure, whereas the patient operated on by the suprapubic route is quite indisposed for a number of days thereafter. Laboratory findings also confirm this. Whereas with the suprapubic method the patient shows a high nonprotein nitrogen for a long time postoperatively, with the perineal method the nonprotein nitrogen is reduced to normal within from four to five days.

The lesser shock of the perineal prostatectomy makes it possible to perform a one-stage operation on patients who are quite weak and those who have disturbed kidney function. By the suprapubic method, such patients must be operated on in two stages often several weeks apart. This division of the operation into two stages has quite a distressing effect on the patient. The first stage of the procedure, the simple cystostomy, appears to him as major, and as dangerous an operation as the second stage in which the complete enucleation of the gland is performed. The necessity of undergoing two operative procedures frequently frightens the patient away from all operative intervention in his disease, or, as I have frequently experienced, drives him to a surgeon who will perform the perineal prostatectomy in one stage.

Perineal prostatectomy offers the additional advantage that the wound heals under more comfortable circumstances. The perineal wound is relatively painless and does not disturb the patient in any respect during respiration and expectoration. A suprapubic wound, under the best conditions, renders each cough and even each breath painful. The patient, therefore, usually breathes very superficially, and may retain detrimental secretions, which makes him more liable to post-

operative pulmonary complications than in perineal cases. Also, the perineal wound drains much better, which accounts for the fact that there are less wound complications or septic symptoms than in the suprapubic method. The immediate postoperative mortality is as small or perhaps even smaller. The perineal prostatectomy restores the anatomic relationships more normally than does the suprapubic method, for by sewing the urethral stump to the neck of the bladder, union between the bladder and the urethra is almost normally reconstructed. The latter fact may be proved later by a urethroscopic examination, when the colliculus seminalis may be seen, and the smooth transition from the urethra into the bladder observed. Also, by means of this perineal method in which the urethral stump is sewed to the bladder, the large pouch formed by the empty prostatic bed, which always remains after suprapubic method, is largely avoided, and the cause for postoperative formation of calculus and infection is prevented. Strictures of the neck of the bladder, which so frequently occur following suprapubic prostatectomy, are never experienced with this perineal method of prostatectomy.

Should it be discovered during the operation that the prostate is carcinomatous, it will be possible without any great extension of the wound to excise the carcinomatous tissue so thoroughly that in 30 per cent of these patients a permanent cure has been obtained. In this respect the perineal prostatectomy is vastly superior to the suprapubic method.

All of these undeniable advantages of perineal prostatectomy lead me, in spite of the improvements attained in recent years in the suprapubic method, to recommend perineal prostatectomy as the method of choice in prostatic hypertrophy. I use the suprapubic method only in those cases in which there is an unusual narrowness of the pelvic outlet, i. e., when the distance between the ischial tuberosities is less than two fingerbreadths, so that an insufficient view of the structures would be obtained by the perineal method, and in cases in which in addition to prostatic hypertrophy there is a bladder condition such as a diverticulum or tumor which alone would demand a suprapubic incision into the bladder.

The fear of postoperative disturbance of sexual potency should no longer prevent one from performing the perineal operation, even in younger patients. Increasing experience strengthens me in the impression that this particular technic of perineal prostatectomy does not disturb the sexual ability any more than does the suprapubic prostatectomy.

It has heretofore been frequently conceded by many surgeons that the reason they did not adopt perineal prostatectomy as a routine procedure was their aversion to its technical difficulties. This timidity

is really unjustified, as will quickly be recognized by those who will decide to perform the operation a number of times. They will quickly come to the conclusion that no great technical dexterity is necessary for its performance, merely a thorough knowledge of the anatomy of the perineum.

SUMMARY

1. The Wildbolz method in comparison with other perineal methods of prostatectomy is presented.

2. The method emphasizes the importance of both urethral sphincters and considers the urethral musculature as a single functional unit.

3. The incision in the prostatic capsule is placed as far as possible toward the bladder.

(*a*) It preserves the sphincters.

(*b*) Incontinence is eliminated.

(*c*) The nerves approaching the prostate gland are left mainly undisturbed.

(*d*) The patient's potency is usually not disturbed.

(*e*) Fistulas almost never occur.

4. Complete anatomic reconstruction of the prostatic region and urethra is carried out.

5. The operation is clearly visualized from beginning to end, thus:

(*a*) Exact hemostasis is possible.

(*b*) It is unlikely that a small piece of adenoma will be left behind.

6. The advantages of routine vasotomy to avoid epididymitis are discussed.

7. Postoperative treatment is outlined.

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CIRCULAR SUTURE OF BLOOD VESSELS

AN EXPERIMENTAL STUDY

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Obstruction of the lumen by blood clotting at the suture line is the chief hazard to the physiologic function of a blood vessel the ends of which have been joined by a circular suture. That this is the greatest risk in repair of a blood vessel is emphasized by many observers. Horsley,[1] Smith,[2] McNealy[3] and Buchanan[4] agreed that thromboses occur after many arterial sutures.

With the Carrel technic in skilled hands, according to Sofoteroff,[5] thrombosis occurs in a large percentage of cases. Moszkowicz[6] feared the circular suture because of thrombosis. A review[7] of the papers on vascular surgery written by important German surgeons and published during the World War reveals that the occurrence of early or progressive thrombosis after operations on arteries is frequent. It is a fair estimate in the opinion of that reviewer that in half of the cases in which a suture is made a viable artery is retained.

Before the World War, Matas[8] collected from the literature records of forty-nine circular sutures which had been performed in civilian

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1. Horsley, J. S.: Surgery of the Blood Vessels, St. Louis, C. V. Mosby Company, 1915.

2. Smith, E. A.: Suture of Arteries: An Experimental Research, London, Oxford University Press, 1909.

3. McNealy, R. W.: Surgery of the Vascular System, Journal-Lancet **47**: 244, 1927.

4. Buchanan, J. J.: Circular Resection and Suture of the Axillary Artery for Transverse Laceration by Fracture: Dislocation of the Anatomical Neck of the Humerus, Surg., Gynec. & Obst. **15**:648, 1912.

5. Sofoteroff: Military Surgery of the Vascular System, cited by Matas, R., in Keen, W. W.: Surgery: Its Principles and Practice, Philadelphia, W. B. Saunders Company, 1921, vol. 7, p. 713.

6. Moszkowicz, L.: Wie vermindern wir die Gefahr des Gangräns nach Aneurysmen-Operationen, Beitr. z. klin. Chir. **97**:569, 1915; abstr., M. Supp., Daily Rev. Foreign Press **1**:402, 1918.

7. M. Supp., Daily Rev. Foreign Press **1**:402, 1918; comments by the editor.

8. Matas, Rudolph, in Keen, W. W.: Surgery: Its Principles and Practice, Philadelphia, W. B. Saunders Company, 1921.

hospitals and under conditions of peace. An analysis of the postoperative evidence revealed that 13.1 per cent had been followed by gangrene. Of the thirty-seven patients who recovered, in no less than thirty-three (87.6 per cent) the anastomosis had proved functionally valueless or superfluous if judged by the behavior of the peripheral pulses. In addition to the liability to occlusive thrombosis in the line of suture, which admittedly occurs in the absence of all infection, as a result solely of the trauma, Matas included the possibility of secondary hemorrhage from infection, panarteritis and the possibility of recurrence by yielding of the suture line as fallacies of direct arterial suture. In his opinion these failures are not overcome by the undoubted surgical successes of the German surgeons during the World War.

It cannot be questioned, in the opinion of La Roque,[9] that skilful suture is often followed by thrombosis, and he added that disappointment is apt to follow the expectation to secure information necessary to the solution of the problems from a study of clinical case reports in the literature. Carrel[10] found that failure is often due to the formation of a thrombus, but this is due to surgical causes,[11] and with the proper technic positive results can be secured.

Secondary hemorrhage as a sequel to arterial anastomoses is infrequent. In a study of twenty-nine instances of arterial suture reported in the literature, Buchanan[4] found no mention of hemorrhage. Aneurysm was not observed in this series, and Reid[12] noted that aneurysms do not develop in interposed venous grafts on arteries. Smith,[2] as well as Matas,[8] stated that aneurysm is a rare sequel to the suture of arteries. Stenosis of the sutured segment may occur from either the contraction of cicatricial tissue or from the organization of a thrombus. Cicatricial stenosis develops gradually. Bier[13] and most of the German surgeons frankly admit the uncertainty of the ultimate fate of the sutured vessel. They contend that even if the lumen at the suture line is ultimately obliterated, the gradual obstruction gives plenty of time for the establishment of ample collateral circulation.

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9. La Roque, G. P.: Ligation of the External Iliac Artery and Vein Above and Below a Communicating Bullet Wound of These Two Vessels, Ann. Surg. **73:** 265, 1921.

10. Carrel, Alexis: The Surgery of Blood Vessels, Bull. Johns Hopkins Hosp. **18:**18, 1907.

11. Carrel, Alexis: Graft of the Vena Cava on the Abdominal Aorta, Ann. Surg. **52:**462, 1910.

12. Reid, M. R., and Andrus, W. DeW.: Surgery of the Arteries, in Nelson Loose-Leaf Living Surgery, New York, Thomas Nelson & Sons, 1928, vol. 1, p. 647.

13. Bier, A.: Chirurgie der Gefässe Aneurysmen, Beitr. z. klin. Chir. **96:**566, 1915; cited by Matas.[8]

EXPERIMENTAL STUDIES

In these studies experiments were made to secure information about the technical causes of failures to preserve the physiologic function of arteries joined by circular suture. Intermittently over a period of many months, arteries and veins of dogs were severed and the ends joined in various conditions of control. After the repair the results were studied within from a few hours to many months by examination post mortem or at reoperation.

Series of Circular Sutures of Superficial Vessels.—In seven strong, medium to large-sized dogs twenty-three end-to-end anastomoses of superficial arteries and veins were made. Each animal was given 1 grain (0.066 Gm.) of morphine sulphate subcutaneously, and anesthesia was produced by sodium iso-amylethylbarbiturate, given intravenously. Through wide exposure the vessels were brought up, the branches or tributaries ligated and the flow of blood interrupted by serrefines, the blades of which were covered by gauze. The vessels were cut by a sharp knife, and the tunica adventitia was removed. The intimal surfaces were cleansed of blood and kept moist by frequent washings with physiologic solution of sodium chloride in 100 cc. of which 1 dg. of heparin had been dissolved.

The solution of heparin used in all our experiments approximates the ideal for an anticoagulant. It has been used clincally in blood transfusions, and the evidence indicates that it may be employed with safety.[14] A water-soluble and thermostabile substance, heparin in solution retained its ability to prevent blood from clotting after four months. During this period it had been subjected on four occasions to 15 pounds (6.8 Kg.) of steam pressure for twenty minutes in the autoclave. Heparin was isolated by Howell,[15] and was described as an antiprothrombin which prevents the calcium of the plasma from activating prothrombin into thrombin.[16] Howell considered that the effect of the thromboplastic substances of injured tissues and of injured blood platelets is to neutralize the antiprothrombin or heparin of the blood. Muscle tissue, when injured, the liver, the lungs and the kidneys are rich in thromboplastic substances. The walls of the blood vessels are especially rich in these "coagulins." [17] Wells [16] recalled that the joint action of the tissues and blood thromboplastic substances is greater than the sum of their individual actions. The heparin solution neutralizes the

14. Reed, C. J.: Practical Uses of Heparin, J. Lab. & Clin. Med. **14**:243, 1928.

15. Howell, W. H.: Purification of Heparin and Its Chemical and Physiological Reactions, Bull. Johns Hopkins Hosp. **42**:199, 1928.

16. Wells, H. G.: Chemical Pathology, ed. 5, Philadelphia, W. B. Saunders Company, 1925, p. 350.

17. Loeb, Leo: Univ. Pennsylvania M. Bull. **16**:382, 1904; cited by Wells.[16]

thromboplastic substances coming from the injured wall of the blood vessel. Its disadvantage is that it may not be available in emergency vascular repair.

The Carrel triangular suture technic was used, with the finest silk and human hair in number 16 straight needles sterilized and kept in liquid petrolatum. Care was used to keep each line on a tension while suturing to prevent narrowing at the suture line. The serrefines were removed promptly when the suture was completed. No secondary sutures

TABLE 1.—*Series of Circular Sutures of Superficial Vessels* *

Animal Number	Vessels Joined by Anastomosis	Date of Operation	Date of Examination	Time, Days	Findings
4	Suture of left common carotid.....	8/10/30	†		
7	Proximal right to distal left carotid..	7/31/30	8/15/30	15	No thrombosis or stenosis
7	Previous anastomosis resected; ends rejoined	8/15/30	11/ 2/30	79	No thrombosis or stenosis
7‡	Anastomosis resected; ends rejoined..	11/ 2/30	1/31/31	90	No thrombosis or stenosis
8	Right femoral cut; ends rejoined.....	8/17/30	10/ 5/30	49	Complete stenosis
8	Proximal right carotid to distal left external jugular vein	8/17/30	10/ 5/30	49	Complete stenosis
8§	Proximal left carotid to distal right carotid	8/17/30	10/ 5/30	49	Complete stenosis
9	Suture of right common carotid.....	8/15/30	9/ 7/30	23	No thrombosis or stenosis
9‡	Anastomosis resected; ends rejoined..	9/ 7/30	12/29/30	113	Complete stenosis
10	Suture of right common carotid.....	8/10/30	9/ 7/30	28	No thrombosis or stenosis
10	Suture of right external jugular vein	8/10/30	9/ 7/30	28	No thrombosis or stenosis
10	Suture of left external jugular vein..	9/ 7/30	11/ 2/30	56	No thrombosis or stenosis
10	Anastomosis right external jugular vein resected; resutured	9/ 7/30	11/ 2/30	56	No thrombosis or stenosis
10	Cross-anastomosis of carotids.....	9/ 7/30	11/ 2/30	56	No thrombosis or stenosis
10	Resection of cross-anastomosis; ends rejoined	11/ 2/30	‡	..	No further examination
11	Proximal right carotid to proximal left external jugular vein	8/17/30	11/ 2/30	77	Complete stenosis
11	Proximal left carotid to distal right carotid	8/17/30	11/ 2/30	77	Complete stenosis
11	Carotid suture removed; ends rejoined	11/ 2/30	1/31/31	90	Complete stenosis
12	Jugular vein transplanted to right carotid	10/ 5/30	11/ 2/30	28	Complete stenosis
12	Left carotid cut; ends rejoined.....	10/ 5/30	11/ 2/30	28	Complete stenosis
12‡	Right iliac vein transplanted to right iliac artery	10/ 5/30	11/ 2/30	28	Complete stenosis

* Sodium iso-amylethylbarbiturate anesthesia was used intravenously throughout. Stenosis was observed in 52.6 per cent of the circular sutures of this series.
† This animal was lost. No further examination was made.
‡ Ordered killed because of epidemic of rabies. No further examination made.
§ This animal died on Oct. 20, 1930. For two days preceding death there was spastic paralysis. On broad surfaces made by sectioning the hardened brain, there were no gross areas of focal necrosis.

were made. After several minutes' observation to see that no thrombosis occurred, the sheath of the vessel was closed, and when convenient, viable muscle was tucked snugly about the vessel.

Examinations of these vessels were made from fifteen to one hundred and thirteen days after operation. Complete stenosis was observed in 52.6 per cent of the vessels examined (table 1). Stenosis in these instances may have followed thrombosis. That this occurred in animal

8 is improbable. Both common carotid arteries supplying the brain were stenosed after forty-nine days. Necrosis of the brain would have followed sudden obstruction by clotting. This did not occur, however, for the animal lived normally until after the segments were removed. On broad surfaces made by sectioning the hardened brain removed at autopsy, no areas of necrosis were seen. In four other instances, for from 2 to 5 cm. on either side of the stenosed suture line, there was freshly clotted blood in the lumen, indicating that complete occlusion had preceded the examination by only a short time.

While proof is lacking, we conclude from our observations that stenosis in these small vessels is often due to the contraction of the dense fibrous capsule or callus that forms outside the vessel at the suture line and extends from 5 to 10 mm. in either direction along its wall. This is not of practical interest, for in clinical surgery vessels of this size would never be sutured.

Series of Circular Sutures of Deep Vessels.—(*A*) End-to-End Anastomoses of the Aorta: The abdominal part of the aorta in medium to large-sized dogs is more nearly the size of vessels usually sutured in man. With the blood circulating through them, their maximum diameter varies from 8 to 11 mm. In fifty-one animals the aorta was exposed through a longitudinal ventral incision, its branches were ligated for 2 cm., and the flow of blood was interrupted by two strips of tape 5 mm. wide passed completely around it, the ends of the tape being held by small pile clamps. In fifty animals the aorta was severed, and the ends were rejoined. In one (animal 27), the central end of the aorta was united to the distal end of the inferior vena cava (table 2).

The aorta was cut by a sharp knife 1 cm. proximal to the origin of the inferior mesenteric artery. The ends of the tunica adventitia were grasped by Graefe plain fixation forceps and as much removed as could be pulled past the ends of the vessel. The blood was carefully washed out, and the intimal surfaces were kept moist with heparin solution. Except as mentioned, all oozing of blood was stopped before proceeding with the suture. In two instances, the Bier-Moure two-point suspension technic [13] was used; in all others, the Carrel prismatic suture was employed. Number 00 chromicized catgut on a curved swedged needle was used for ten sutures; for the remainder, black waxed A silk on Carrel curved blood vessel needles. Prepared in phenolized beeswax after the manner devised by Moses Gunn and described by McArthur,[18] the silk is smooth and solid like silkworm gut, is stronger than before waxing and is much more easily handled in deep wounds.

18. McArthur, L. L.: Preparation of Waxed Silk, Surg., Gynec. & Obst. **16**: 460, 1913.

In our work we made this departure from the original Carrel technic: To form the posterior point of the triangle we placed two traction sutures through the edges of the vessel and closely together in the back wall. The ends of one were brought out to the right, the ends of the other, to the left, of the vessel. Time is saved when working in a deep wound by not having to pass the traction suture behind the vessel. Moreover, the artery need not be freed from its collateral vessels for so great a distance. Thus, the collateral circulation is better preserved. The importance of this is stressed by Bier, Matas [8] and Makins, for if gradual thrombosis or stenosis should occur, the uninjured collaterals might assume the function of the obstructed vessel.

The ends of the artery are apposed by tying the retaining stitches. An end of one of the posterior retention sutures is threaded into the needle, and a side of the triangle is sutured. Instead of tying the stitch to the traction thread at each corner as suggested by Bernheim,[19] we discovered that a lock stitch is much better. The last stitch of the line, taken 1 mm. from the traction suture, is the lock stitch. This prevents the line of suture from loosening or from being drawn too taut by subsequent pulling. When the second posterior traction suture is reached, the continuous suture is tied to one of its ends. The suture line is then carefully inspected; accessory sutures are taken if needed, and the flow of blood is reestablished. The distal tape is removed first, and the proximal as quickly as possible. Bleeding will occur, but a sponge pressed tightly will control it. A thin strip of muscle held closely to the suture line, as suggested by Bird,[20] hastens clotting in the needle holes. When the bleeding stops, the ends of the tunica adventitia are brought over the suture line by interrupted stitches, the vessel sheath closed and the edges of the peritoneum apposed.

In this study we are interested chiefly in thrombosis complicating the circular suture of the blood vessels. Before proceeding further, some of the etiologic factors of thrombosis will be considered. Aschoff [21] reminded us that there is not a single cause but a number of different conditions which are closely interrelated in the occurrence of thrombosis:

1. The factor of trauma. Traumatic injury to the intima is an important element, but McLean [22] has shown that endothelial damage per se is not a cause of thrombosis. He crushed the veins of dogs and repeated the procedure in forty-eight hours, yet was unable to produce

19. Bernheim, B. M.: Surgery of the Vascular System, Philadelphia, J. B. Lippincott Company, 1913.

20. Bird, C. E.: Anastomosis of Veins, Surg., Gynec. & Obst. **42**:428, 1926.

21. Aschoff, L.: Lectures on Pathology, New York, Paul B. Hoeber, Inc., 1924.

22. McLean, Angus: Thrombosis and Embolism, Surg., Gynec. & Obst. **20**: 457, 1915.

thrombosis at the site of repeated crushing. Murphy [23] observed that arteries penetrated by bullets rarely become occluded by blood clots.

2. The element of stasis and slowing of the blood stream. Stasis of the blood stream of itself does not produce thrombosis. This has been shown by the famous living test tube experiments of Hunter and Durante,[24] Glenard and others. Blood in a segment of artery or vein between two sterile ligatures remains fluid for hours, days and weeks. Welch, in his classic monograph on thrombosis,[25] expressed the opinion that slowing of the blood stream is not a sufficient cause, but is important when combined with other factors such as trauma and infection. In certain experiments in extracorporeal thrombus formation performed on rabbits, Rowntree and Shionoya [26] found that the conditions tending to retard the circulation hastened the progress of clotting. Conversely, when circulatory stimuli such as thyroxine and ephedrine were injected into the animals, the circulation was maintained longer than normal.

3. The factor of infection. Infection may play a rôle in thrombosis. The experiments of McLean [22] are instructive. After crushing the wall of a vein he introduced a twenty-four hour bouillon culture of Staphylococcus aureus into the vein and again crushed it to work the organisms into its walls. No thrombi were found at the site of the injury. Sterile threads were suspended in the veins, and no clots formed on them. When threads infected by soaking in cultures of bacteria were suspended in the veins, clots formed and occluded their lumens.

4. Changes within the blood. Lee and Vincent,[27] by experiments, showed that the coagulation time depends on the number of blood platelets present. Welch [25] observed that the platelets are increased in chlorosis of which thrombosis is a well recognized complication. Hueck [24] noted a marked increase in the platelet count up to about the thirteenth day after operation, depending on its severity. Dawbarn and his associates [28] obtained similar results. They found that the number of plate-

23. Murphy, J. B.: Resection of Arteries and Veins Injured in Continuity: End to End Suture, M. Rec. **51**:73, 1897.

24. Cited by Hosoi, K.: Postoperative Thrombosis, Pulmonary Embolism and Infarction, Internat. S. Digest **13**:67, 1932.

25. Welch, W. H.: Thrombosis, in Albutt, T. C., and Rolleston, H. D.: A System of Medicine, New York, The Macmillan Company, 1899, vol. 7, p. 153.

26. Rowntree, L. G., and Shionoya, T.: Studies in Experimental Extracorporeal Thrombosis, J. Exper. Med. **46**:7, 1927.

27. Lee, R. I., and Vincent, B.: The Coagulation of Normal Human Blood: An Experimental Study, Arch. Int. Med. **13**:398 (March) 1914.

28. Dawbarn, R. Y.; Earlam, F., and Evans, W. H.: Relation of the Blood Platelets to Thrombosis After Operation and Parturition, J. Path. & Bact. **31**:833, 1928.

lets begins to rise on the sixth day, reaches a maximum about the tenth day after operation and persists for a further four or five days, normal figures being reached in about three weeks. Gage,[24] who reviewed the literature on blood platelets, concluded that the platelet count in the circulating blood reaches its highest about the time of the appearance of clinical thrombosis. Tissue fibrinogen, given subcutaneously or by mouth, also alters the blood so as to shorten the clotting time.[29]

In all of these experiments the element of injury was present. In thirty-three, sodium iso-amylethylbarbiturate was given intravenously for anesthesia. When used intravenously in clinical surgery, observers [30] find a reduction in the blood pressure. In one series,[31] the systolic pressure was reduced an average of 46 mm. of mercury; the diastolic, 23 mm. No measure of the blood pressure in these animals was made, but a profound anesthesia was maintained, in many, until death of the animal occurred. Nineteen were killed and examined within forty-eight hours. In ten of these thrombosis was found; in eight, the thrombus obstructed the lumen. Early in our studies we found that thrombosis could be predicted definitely because of slight oozing of blood from a collateral not properly ligated. We have denoted these as anticipated thrombi. Six of the occlusive thrombi were anticipated, leaving two instances of unexplained occlusive thrombi occurring with this anesthetic. Ether anesthesia was used eighteen times. Thrombi were found four times; an obliterating clot was found once, and its occurrence was predicted. Of this series of fifty-one animals, five were not examined because of extensive postmortem changes.

In sixteen animals from 2 to 6 cc. of fibrogen, a purified tissue fibrinogen, prepared and furnished by the William S. Merrell Company, was given intramuscularly one hour before operation. No determinations of the clotting time were made. In each instance a quick clotting reaction of the blood was noted. This tissue fibrinogen was used in seven animals having sodium iso-amylethylbarbiturate anesthesia and in nine having ether anesthesia. One of the sixteen animals was not examined. Occlusive thrombosis occurred once with each anesthetic, and in both the clotting was anticipated.

Infection was the cause of death in seven animals. In two of these it was induced. For one (animal 71), from a twenty-four hour bouillon culture of Staphylococcus aureus, sufficient was taken to fill the segment

29. Mills, C. A.: Do Blood Platelets, Plasma and Tissues Yield Thrombin, or Tissue Fibrinogen? Am. J. Physiol. **95**:1, 1930; Considerations of the Problem of Blood Clotting, Am. J. M. Sc. **172**:501, 1926.

30. Sise, L. F.: Intravenous Sodium Isoamylethyl Barbiturate with Spinal Anesthesia, Am. J. Surg. **9**:65, 1930.

31. Ranson, B. B., Jr., and McLellan, G. A.: Induction Anesthesia by Sodium Amytal, Am. J. Surg. **9**:60, 1930.

of aorta and to bathe the suture line during the suturing. The toxins of Staphylococcus aureus produce clotting more readily than those of other organisms examined by Loeb,[32] while those of Bacillus coli have an intermediary place. In another animal (number 73), a small gauze sponge infected with floor dirt was placed outside the suture line next to the aorta. A violent peritonitis occurred in five others. At autopsy, from two to thirteen days after operation, no endovasal thrombi were found in any of the animals. Four of these animals had received sodium iso-amylethylbarbiturate anesthesia.

Of the twenty-four animals having sutures of the deep vessels, including the venous transplants, examined or living after one month, in only one (number 13) was an aneurysm observed (4.1 per cent) and in another (number 10), stenosis (4.1 per cent). Chromicized catgut was the suture, and, when absorbed, the suture line relaxed, producing a small saccular aneurysm 8 mm. in diameter. In clinical surgery one would not use chromicized catgut. When the eleven sutured with chromicized catgut were examined, obstructing thrombi were found in two. Each of these was anticipated because of blood oozing from the ends of the aorta.

Stenosis (number 10) was produced by the organization of a slowly forming obliterative thrombus. The protocol for this animal follows.

ANIMAL 10.—On June 20, 1931, the aorta was cut, and the ends were joined by number 00 chromicized catgut. There was a good femoral pulse on the following day. On June 29, the animal was active, but the femoral pulses were weak. On July 3 and 23, no femoral pulse could be felt. On May 7, 1932, there were strong femoral pulses. The abdomen was opened and the aorta exposed. A segment of the aorta 4 cm. long was removed, 2 cm. of which was a fibrous cord. There was a good collateral circulation. A piece of the right external jugular vein was transplanted to fill the gap.

(*B*) Transplantation of Venous Segments to the Aorta: Segments of veins were grafted to the abdominal aorta in twenty-nine dogs. In six the site of a previous anastomosis was removed. But for one ether anesthesia was used throughout. The tissue fibrinogen, fibrogen, was given to five. The triangular suture of black waxed A silk was used. Great care was taken to evert the edges of the veins. To best secure eversion, we placed the retaining stitches as "mattress-on-edge" sutures. The tissue "coagulins" were neutralized and the intimal surfaces cleansed and moistened by the solution of heparin. Intravascular clotting is more favored by conditions found in venous grafting. On examination post mortem, thrombi were found in fourteen of the twenty-seven animals; two of the animals are living. In five segments the lumen was completely obstructed. Three of the five clots were anticipated (table 2).

32. Loeb, Leo: The Influence of Certain Bacteria on the Coagulation of Blood, J. M. Research **10**:407, 1903.

TABLE 2.—*Series of Circular Sutures of Deep Vessels*

Group A: End-to-End Anastomoses of the Aorta (51 Dogs)

Animal Number	Ether	Sodium Iso-Amylethylbarbiturate	Fibrogen	Thrombosis: Of Any Degree	Thrombosis: Occlusive	Thrombosis: Anticipated	Time Interval Between Operation and Examination: Less Than 24 Hours	24 Hours	48 Hours	72 Hours	4 Days to 1 Month	1 to 6 Months	6 Months or More	Infection	Absorbable Suture	Aneurysm	Stenosis	Hemorrhage	No Examination	Living
1	..	+	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
2	..	+	..	+	+	+	..	..	+	..	..	..	..	..	..	..	..	..	..	..
8	..	+	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
9	..	+	..	..	..	..	..	..	..	..	..	..	..	..	+	..	..	..	+	..
10	..	+	..	..	..	..	..	..	..	..	..	..	+	..	+	..	+	..	..	..
11	..	+	..	..	..	..	..	..	+	..	..	..	..	..	+	..	..	..	..	..
12	..	+	..	+	+	+	..	+	..	..	..	..	..	..	+	..	..	..	..	..
13	..	+	..	..	..	..	..	..	..	..	..	..	+	..	+	+	..	..	..	..
14	..	+	..	..	..	..	..	..	..	..	+	..	..	..	+	..	..	..	..	..
15	..	+	..	..	..	..	..	..	..	+	..	..	..	+	+	..	..	..	..	..
16	..	+	..	+	+	+	..	..	+	..	..	..	..	..	+	..	..	..	..	..
17	..	+	..	+	+	..	..	+	..	..	..	..	..	..	+	..	..	..	..	..
18	..	+	..	+	..	..	+	..	..	..	..	..	..	..	+	..	..	..	..	..
19	..	+	..	..	..	..	..	..	..	..	+	..	..	+	..	..	..	..	..	..
20	..	+	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..
21	..	+	..	+	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
22	..	+	..	+	..	+	..	..	..	..	..	+	..	..	..	..	..	..	..	..
23	..	+	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
24	..	+	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..	..
25	..	+	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
26	..	+	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
27	..	+	+	+	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
28	..	+	+	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
29	..	+	+	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..
30	..	+	+	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..
31	..	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	..
32	..	+	+	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..
33	..	+	+	..	..	..	..	..	+	..	..	..	..	+	..	..	..	..	..	..
34	..	+	+	..	..	..	..	..	..	..	+	..	..	+	..	..	..	..	..	..
35	..	+	..	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..
36	..	+	..	+	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
37	..	+	..	+	+	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..
38	..	+	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..
39	+	..	+	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..
40	+	..	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..
41	+	..	..	+	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..
42	+	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..
43	+	..	+	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..
44	+	..	+	..	..	..	..	..	..	..	+	..	..	+	..	..	..	+	..	..
45	+	..	+	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..
47	+	..	+	+	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..
48	+	..	+	..	..	..	..	..	..	..	+	..	..	..	..	..	..	+	..	..
49	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	..
50	+	..	+	+	+	+	..	..	+	..	..	..	..	..	..	..	..	..	..	..
51	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	..
52	+	..	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..
54	+	..	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+	..
55	+	..	+	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..
60	+	..	..	+	..	+	..	+	..	..	..	..	..	..	..	..	..	..	..	..
71	+	..	..	..	..	..	..	..	+	..	..	..	..	+	..	..	..	..	..	..
73	+	..	..	..	..	..	..	..	..	..	+	..	..	+	..	..	..	..	..	..

Group B: Transplantation of Venous Segments to Aorta (29 Dogs)

4	..	+	..	+	..	..	..	..	..	..	+	..	..	..	..	..	..	+	..	..
7	+	..	..	..	..	..	+	..	..	..	..	..	..	..	+	..	..	..	..	..
10	+	..	+	+	+	+	..	+	..	..	..	..	..	..	..	..	..	..	..	..
13	+	..	..	+	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..
29	+	..	+	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
30	+	..	+	+	+	..	..	+	..	..	..	..	..	+	..	..	..	..	..	..
35	+	..	..	+	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
53	+	..	+	+	..	..	..	..	..	..	+	..	..	..	..	..	..	+	..	..
55	+	..	+	..	..	..	..	..	..	+	..	..	..	+	..	..	..	+	..	..
56	+	..	..	+	+	+	..	+	..	..	..	..	..	..	..	..	..	..	..	..
57	+	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	+	..	..
58	+	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
59	+	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
61	+	..	..	+	..	..	..	..	..	..	+	..	..	+	..	..	..	..	..	..
62	+	..	..	+	..	..	..	..	..	..	+	..	..	..	..	..	..	+	..	..
63	+	..	..	+	..	..	..	..	..	..	+	..	..	+	..	..	..	..	..	..
64	+	..	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..
64A	+	..	..	+	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..
65	+	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
66	+	..	..	+	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
66A	+	..	..	+	..	..	..	..	..	..	+	..	..	+	..	..	..	..	..	..
67	+	..	..	+	+	+	..	+	..	..	..	..	..	..	..	..	..	..	..	..
68	+	..	..	..	..	..	..	..	..	..	..	+	..	+	..	..	..	..	..	..
69	+	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	+	..	..
70	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+
72	+	..	..	..	..	..	..	..	..	..	..	+	..	+	..	..	..	..	..	..
74	+	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
75	+	..	..	+	+	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..
76	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	+

Eddying Currents of von Recklinghausen.—This was observed in the following experiment.

ANIMAL 61.—On Dec. 5, 1931, the abdominal part of the aorta was severed, 1 cm. was removed, and 1.5 cm. of the inferior vena cava was grafted into the gap. The animal died from peritonitis on December 9. At autopsy, the suture lines of the vessels were intact. Molded to the shape and size of the graft and tightly attached to each line of suture was a firm cylindric clot with a lumen 5 mm. in diameter.

Another instance parallel to this was found (animal 4). Although not in itself sufficient to cause thrombosis, von Recklinghausen [33] attached more importance to the whirling or eddying motion than to mere slowness of the circulation. Eddies are produced when blood enters normal or pathologic, dilated channels from small ones. The external jugular vein has a diameter about equal to that of the aorta. No cylindric thrombi were found within those pieces (in all, twenty-three) of external jugular vein grafted to the aorta. To avoid the eddying currents, a vein smaller than that accompanying the injured artery should be used for grafts.

The Deliberate Removal of Obstructing Tapes.—This was carried out on the following animal:

ANIMAL 10.—On May 27, 1932, the obstructed fibrous segment of the aorta, sutured with number 00 chromicized catgut on June 20, 1931, was removed, and a piece of the right external jugular vein was transplanted to its place. When the suturing was completed, the distal obstructing tape was released. Oozing from the suture line occurred for sixty seconds before the proximal tape was removed. The femoral pulse was weak when the abdomen was closed. At postmortem examination twenty-four hours later, there was a firm clot completely filling the segment of vein. This is illustrative of similar other observations.

Following a venous graft on the aorta, the lines of the completed suture are carefully inspected and complementary stitches taken if needed. An immediate release of the full pulsating current is made. According to Howell's hypothesis, clotting does not occur when the flow is rapid, for ample antiprothrombin is carried to neutralize the "coagulins" where liberated. Eberth and Schimmelbusch [34] found that under normal conditions the platelets circulate with red corpuscles in the axial blood current, but make their appearance in the outer still zone, which is from eight to twenty times slower when the rapidity of the circulation is sufficiently diminished. Each thrombus starts as a white thrombus, and its building stones are the blood platelets. The adhesive surfaces of the intima injured at the suture line inflict dam-

33. von Recklinghausen: Handbuch der allgemeinen Pathologie des Kreislaufs und der Ernährung, Stuttgart, 1893; cited by Welch.[25]

34. Eberth, C. J., and Schimmelbusch, C.: Die Thrombose nach Versuchen und Leichenbefunden, Stuttgart, Ferdinand Enke, 1888; cited by Welch.[25]

ages on the platelets. The forceful pulsating current in the artery prevents adhesions of the platelets or the accumulation of formed elements at the site of injury. Hence, every effort should be made to restore the forceful current before the nidus of a clot is formed by stagnant blood. Welch [24] noted that a clot itself is a foreign body and may lead to a further extension of a thrombus. Thrombi seem to have certain self-propagating powers.

Effects of the Valves.—Valves in two of the grafts on the aorta were responsible for clots partly obstructing the flow of blood. In one, placed so as to retard the current, a clot was attached to the proximal suture line, half filled the lumen and extended to a cusp of the valve. In the other, turned so that the blood current kept the valves open, mural thrombi formed behind each cusp. Grafted segments should be implanted so that their valves are kept open by the current of blood; that is to say, the central end in the venous system should become the distal end in the arterial circuit.

Injury to the Intima.—Shaggy, scalelike mural thrombi, from 5 to 7 mm. in diameter, were found in three grafts. None was obstructive. About one-fourth the intima in one piece of vein was covered by these flat plaques of blood clot. Gentleness in handling the vein is imperative. Forceful sponging during its exposure is to be avoided. The intima is kept moist at all times. The influence of the smooth nonadhesive endothelium is of first importance in maintaining fluidity of the blood. Endothelial cells altered by injury may act as foreign substances and induce small mural thrombi to form.

Infection.—The following experiment was carried out:

ANIMAL 30.—On May 4, 1932, under ether anesthesia, 2 cm. of the right external jugular vein was grafted on the aorta. One end of a thread dipped in a twenty-four hour bouillon culture of Bacillus coli was suspended in the vein. The abdomen was closed, and in twenty-four hours the animal was killed. A pear-shaped clot with the thread in its center filled the vessel. There was no attachment to either line of anastomosis.

This experiment confirms the findings of McLean.[22]

In another animal (number 55), after completing the suture, fluid from a twenty-four hour broth culture of Bacillus coli was held in the repaired vessel for two minutes. After forty-eight hours, the animal was killed. There were no clots.

COMMENT

Of the causes generally recognized in the etiology of thrombosis, trauma is a constant factor in repair of the vessels. Alteration in the rate of flow of the blood current plays a more important rôle than is usually considered. Occlusive thrombosis can be predicted with great

accuracy when blood sluggishly oozes from the terminals of the vessel. Heparin solution, unless applied constantly, is powerless to prevent it. Similarly, blood sluggishly flowing from a gradual release of the circulation will in a few seconds congeal enough to vitiate the repair. There is a natural reluctance of the operating surgeon to establishing the full flow of blood until he sees what happens at the line of suture. This reluctance should be overcome. Watson and Makins [35] suggested placing a rubber drainage tube between the tape and the artery to protect the artery from injury by the tape. This has another commendable feature. The rubber tube serves as a guide for the scissors so that the tape can be cut quickly, at once releasing the full flow of blood. A rapid return of the pulsating current prevents damage to the formed elements and dilutes or neutralizes the thromboplastic substances of the tissues. Grafts should be the diameter of the repaired artery and constricted suture lines avoided in order to prevent eddying currents.

In our studies it does not appear that clotting is appreciably influenced by any changes in the rate of flow resulting from profound anesthesia with sodium iso-amylethylbarbiturate. It is our opinion that the nidus of most thrombi forms in the short interval between the time blood enters and the time of the establishment of the free forceful flow through the repaired vessel. Gradual obliterative thrombosis probably results from the self-propagation of this original nidus.

The rôle accorded infection in thrombosis complicating vascular surgery has been overemphasized. No clotting occurred even when the vessels were inoculated with pure cultures. Infections in other parts of the body, viz., a virulent peritonitis and infections of the areolar tissues of the abdominal wall, produced no intravascular clots. The strictest asepsis should be practiced, for an infected suture line leads to necrosis and hemorrhage, which are more serious than thrombosis. That suture should be attempted in the presence of infection of a wound is questionable, but instances are reported by German surgeons with a successful outcome.

There is no evidence from our studies that changes within the blood enhanced clotting in the least. Efforts were not made to measure the changes in the numbers of platelets after operation. According to the observations of Dawbarn and his associates,[28] there was increase in the platelets on the sixth day. Assuming that the platelet count rose in the same way in the animals of our series, this had no influence on the clotting. Obstructive thrombosis did not occur in thirty-five of thirty-seven animals that lived seventy-two hours or longer (two remain alive). While tissue fibrinogen (table 3), given to a small number, noticeably quickened clotting, it did not influence the intravascular clotting.

35. Watson and Makins, cited by Matas.[8]

Segments removed from animals 29, 30 and 55, seven and one-half, seven and one-half and six months, respectively, after operation, were hardened and sectioned. Sections stained according to Weigert's method were studied. There is no evidence that the elastic elements of the tunica media are being substituted for the fibrous scar tissue. Likewise, Neff [36] and Reid [12] found that there is only a fibrous union.

Carrel [11] observed that the vein transplanted on an artery reacts against the increase of blood pressure by thickening of its walls. Veins follow the law of adaptation of an organ to function and can fill the

TABLE 3.—*Data Pertaining to Use of Fibrogen* *

Animal Number	Ether	Sodium Iso-Amylethyl-barbiturate	Thrombosis	Thrombosis Predicted	Occlusive Thrombosis	No Autopsy
Group A: End-to-End Circular Sutures of the Aorta (16 Instances)						
27	..	+	+	+	+	..
28	..	+	..	..	..	..
29	..	+	..	..	..	..
30	..	+	..	..	..	..
32	..	+	..	..	..	..
33	..	+	..	..	..	..
34	..	+	..	..	..	..
39	+	..	..	..	..	..
43	+	..	..	..	..	..
44	+	..	..	..	..	..
45	+	..	..	..	..	..
47	+	..	+	..	..	..
48	+	..	..	..	..	..
50	+	..	+	+	+	..
54	+	..	..	..	..	+
55	+	..	..	..	..	+
Group B: Transplantation of Venous Segments into Aorta (5 Instances)						
10	+	..	+	+	+	..
29	+	..	..	..	..	..
30	+	..	+	+	+	..
53	+	..	+	..	..	..
55	+	..	..	..	..	..

* Used intramuscularly in amounts of from 2 to 6 cc.; no increase in thrombi formation resulted from the use of fibrogen. The use of fibrogen combined with sodium iso-amylethyl-barbiturate anesthesia caused no increase in thrombi formation.

rôle of arteries when necessary. Matas [37] noted that veins have great tolerance for trauma, while Reid [12] stated that veins adapt themselves much more readily to mechanical disturbances than do arteries. Examined after from four to eight weeks, there was no stretching of the wall of the veins implanted on the arteries in animals 64, 68 and 72. Moreover, their walls were thick, with fibrous tissue proliferation from the sheath of the vessel. Veins subjected to the increased blood pressure that is usual in arteries should be observed for from eight to ten years. The surgical literature contains no record of such observations. Placed in their natural habitat on the farm, animals 70 and 76 will be observed, it is hoped, for a few years.

36. Neff, J. M.: Blood Vessel Suture, Surg., Gynec. & Obst. **33**:657, 1921.

37. Matas, Rudolph: The Suture in the Surgery of the Vascular System, Tr. M. A. Alabama, 1905, p. 245.

CONCLUSIONS

1. Surgical trauma and retardation or distortion of the blood current are the chief contributing factors to the thrombosis that occurs where blood vessels are sutured.

2. Infection plays a minor rôle as a cause of blood clotting at the suture line. Careful asepsis is essential to preclude breaking down of the suture line.

3. An obstructing thrombus, when it occurs, usually forms within a few hours after vascular repair. It is secondary usually to platelets deposited before the full flow of blood is released.

4. The increase in blood platelets does not reach its maximum until a few days after operation, usually too late to influence thrombosis in the segment of repair.

5. Heparin solution fulfils the requirements of a satisfactory anticoagulant in suture of the blood vessels.

6. A method of suturing is described which requires the ligation of a minimum of the collateral circulation.

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STAINING OF CARTILAGE

GROSS STAINING BY INTRA-ARTICULAR INJECTION OF DYES IN ANIMALS

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We have been able to find only two articles on the gross staining of cartilage in addition to those already reviewed.[1] A modification of the Lundwall method by Moreira da Rocha[2] referred to the staining of cartilage by methylene blue (methylthionine chloride, U. S. P.), toluidine blue, methyl violet, methyl green and safranin. Staining of joint cartilage was referred to only by implication; staining in the closed joint was not discussed. The author concluded that "no matter the stain used, its electivity for staining and its stability are in direct ratio not only to the maturity of amorphous ground substance of cartilage but also to its quantity." Thus it is found that adult hyaline cartilage will stain better and more strongly than embryonal cartilage of any type or adult cartilage of elastic or fibrous type. Da Rocha stated that this method of studying cartilage is better than desiccation or maceration. This study is, of course, of fundamental collateral interest. Crowe[3] injected isamine blue intravenously, and on killing the animal (rabbit) two days later noted a selective staining of diseased areas in the cartilage in streptococcic arthritis (experimentally produced). Marrow was also stained. In the specimens shown us by Dr. Crowe, there were definite staining of marrow and uniform staining of joint cartilage, but no definitely diseased areas in cartilage were seen. The stained cartilage was a light, clear blue.

METHOD

In this study we have further noted the action of dyes on joint cartilage, with special reference to selectivity of staining of diseased areas in cartilage. In general our experimental course has been this:

From the Laboratory Division, Hospital for Joint Diseases.

1. Burman, M. S.: The Selective Staining of Diseased Areas in Cartilage by the Intra-Articular Injection of Dyes, with Special Reference to Arthroscopy: An Experimental Cadaver Study, Arch. Surg. **26**:153 (Jan.) 1933.

2. Moreira da Rocha, J.: Staining of Adult Cartilage by Lundwall's Method, Anat. Rec. **13**:447, 1917.

3. Crowe, H. W.: Streptococcal Lesions in Rabbit Demonstrated by Intra-Vital Staining, Tr. M. Soc., London **53**:94, 1930; personal communication.

In one group of animals (rabbits and guinea-pigs), the dye chosen was injected into the knee joint under amytal anesthesia (70 mg. per kilogram of body weight injected intraperitoneally). Occasionally it was necessary to support the amytal with ether. The joints into which injections had been made were examined either immediately or from two to nine days later, to determine the fate of the dye and the gross reaction of the joint to the dye. In most cases, the abdomen was opened and the retroperitoneal region exposed to the action of filtered ultraviolet radiation (Wood's light) to see if there was any absorption of the dye by the lumbar lymph nodes.[4] In no case were we able to demonstrate dye in the glands. In a second group of animals (rabbits only), the cartilage was traumatized by injuring the cartilage and synovia of the knee joint by the insertion of a large bore needle into the closed joint. It is not difficult to localize the point of the needle, and one can easily feel what structures are being injured. It is necessary to use force to create a defect in cartilage, always a bit more force than one thinks is required. This method is simpler than, and as sure as, the more time-consuming method of open operation (Key[5]). At a varying interval after the operation, injections of the dye chosen were made into the knee joint. The joint was then opened at once.

Choice of Dyes.—It is obvious that the use of alcoholic dye solutions intra-articularly is contraindicated; hence all the dyes used were dissolved in water. The relation between the p_H of the dye and that of the joint fluid and the resultant staining was not studied. In fact, it is very difficult to obtain even a drop of synovial fluid from these small joints for examination. The joint is simply moist, and there is no accumulation of fluid. The amount of dye injected was usually not more than 2 cc., 0.5 or 1 cc. often being enough to distend the joint. One should make the injection with the needle in the quadriceps bursa, the needle being held parallel to the bursa. It is sometimes difficult to enter the joint, but easy flow and withdrawal of dye indicate that the joint is being distended. The distention of the quadriceps bursa may at times also be felt. Occasionally a little of the dye will appear subcutaneously, owing possibly to the sharp bevel of the needle. One should guard against fascial and intermuscular injection of the dye.

Both acid and basic dyes were used. Dyes were selected from the most important groups of dyes, the chromophore grouping, which is here outlined (after Conn[6]), being used.

Dyes Grouped by Chromophores

1. Nitro dyes
2. Azo dyes
3. Oxyquinone dyes
4. Quinone imide dyes
   - (*a*) indamins
   - (*b*) thiazins
   - (*c*) oxazins
   - (*d*) azins, which include
     - (1) amido-azins
     - (2) safranins
     - (3) indulins

4. Rynearson, E. H.: The Macrophage in Absorption from the Synovial Cavity, J. Bone & Joint Surg. **13**:127, 1931. Kuhns, J.: Lymphatic Drainage of Knee and Ankle Joints, J. Bone & Joint Surg. **11**:412, 1929.

5. Key, J. A.: Experimental Arthritis: The Changes in Joints Produced by Creating Defects in the Articular Cartilage, J. Bone & Joint Surg. **13**:725, 1931.

6. Conn, H. J.: Biological Stains: A Handbook on the Nature and Uses of the Dyes Employed in the Biological Laboratory, ed. 2, Geneva, N. Y., Commission on Standardization of Biologic Stains, 1929.

5. Phenylmethane dyes
   (*a*) *di*-phenylmethanes
   (*b*) *di*-amino-*tri*-phenylmethanes
   (*c*) *tri*-amino-*tri*-phenylmethanes
   (*d*) hydroxy-*tri*-phenylmethanes
6. Xanthine dyes, including
   (*a*) pyronins
   (*b*) rhodamines
   (*c*) fluorane derivatives
   (*d*) phenolphthaleins and sulphonphthaleins

Trypan blue is an acid azo dye. Of the oxyquinone group, alizarin, which is almost insoluble in water, was used, purpurin not being available. Of the thiazin subgroup of the larger quinone imide group, methylene blue was used. Toluidine blue was not employed in this series of experiments, having previously been noted as a dye which stains cartilage uniformly. Of the amido-azin subgroup, neutral red was used; it had previously been indicated as a possible selective dye. Of the safranins, safranin O was used. Janus green is an azo dye, as well as an azin, and is related to safranin. Gentian violet and aniline blue represented the tri-amino-tri-phenyl methanes. Isamine blue (also called pyrrhol blue, Ehrlich) is a sulphonated tri-beta-naphthyl-pararosanilin, and hence belongs in this group. The fluoranes were represented by eosin and mercurochrome. Alum carmine, a cochineal derivative, was the only natural dye used. Lithium carmine was not used.

The nitro dyes, as picric acid, were not tested. Of the azo dyes, Bismarck brown and sudan III had previously been used and shown to be quite ineffectual in staining cartilage. The other dye groups were not used, because the dyes within the groups were not available. The phenolphthaleins and sulphonphthaleins are indicators and hence were not used. The effect of litmus was noted previously.

RESULTS

Effect of Dyes on Normal Joints.—Six knee joints of three guinea-pigs were studied. A 1 per cent solution of isamine blue was injected into two knees; one was examined at once, and one three days later. A 0.5 per cent solution of gentian violet was injected into one knee; the joint was examined at once. A 1 per cent solution of mercurochrome was used in three knees; in one case, the knee was examined at once; in the other cases, one and two days after injection, respectively.

The stains dyed cartilage uniformly and superficially over a wide area. The stains were not washed away on rinsing. All other structures in the joint, such as synovia and menisci, were also stained, though possibly less uniformly. Some of the intra-articular structures, such as the crucial ligaments, stained with difficulty. Three of the joints were examined immediately after injection, and three from two to three days later. The intensity of staining had become less, and the uniformity of staining more patchy, which indicated either absorption of the dye or wearing away by movement of the joint. No reaction to these dyes was noted, either in cartilage or in synovia; no exudate was present. In two cases, the dye did not enter the joint cavity proper

but was in the muscle and fascia. It should be noted that mercurochrome-220 soluble, which is closely akin to eosin, did stain cartilage uniformly. This point will be discussed again.

The dyes chosen were also injected into six knee joints of three rabbits. A 1 per cent solution of isamine blue was used in one knee; the joint was examined one week later. A 1 per cent solution of mercurochrome was used in one case; this joint was examined one week later. A 1 per cent solution of gentian violet was injected into two joints; the knee joints were examined three and nine days later, respectively. A 1 per cent solution of methylene blue was injected into two knee joints. Examination was made three and nine days later, respectively.

No attempt was made to change the strength of solution previously used. All these dyes stained normal, healthy cartilage. It was noted that the intensity of staining diminished as the dye remained in the joint longer, the dye being distributed unevenly. In the case of gentian violet, it was noted that the posterior part of the femoral condyles was still well stained three days after injection, but that the posterior compartment of the knee showed a bluish granular débris, a possible evidence of synovial irritation. In a joint into which injection of methylene blue had been made an accidental suppurative arthritis developed, confined to the anterior aspect of the joint. There was no suppuration in the posterior compartments, and the dye was still present over the posterior part of the femoral condyles. Synovia and other intra-articular structures stained well, especially with gentian violet.

It is thus seen that the immediate effect of these dyes is a uniform, superficial staining of cartilage and synovia, without particular irritation. All parts of joint cartilage do not stain equally well, those more accessible to the dye staining better. Thus the tibial condylar cartilage usually did not stain well. As time passed, and even as early as the second or third day after injection, there was a gradual disappearance of the dye from the joint, so that no dye or possibly only patchy areas of dye-stained cartilage were present. All the dyes used, in the particular concentrations noted, stained cartilage uniformly, and there was no selectivity of staining.

Effect of Dyes on Experimentally Traumatized Joints.—Into eighteen knee joints of nine rabbits various dyes were injected as tabulated (table), the joints having been traumatized experimentally as previously described. At varying intervals after the initial trauma, the dye chosen was injected into the joints. The joints were opened at once to determine the effect of the dye, with particular reference to selectivity of staining.

It is not necessary to go into any detailed gross and microscopic examination of these traumatized joints. The work agrees in general

with the results reported by Key. Whether the alterations within the joint produced by trauma can be strictly called arthritis is an important point, especially from the standpoint previously enunciated that natural arthritic erosions stain selectively. Usually, synovial hypertrophy and synovial adhesions were present; in some cases, the synovial adhesions were so marked that it was not possible to inject the dye into the joint. The areas of damage originally inflicted by the needle either were superficial or reached to the bone marrow. Many of the lesions, especially the more recent ones, were covered with fibrin. There was no tendency toward repair of these traumatic defects in cartilage or toward enlargement of these areas. In some cases, as noted by Key, there was a tremendous overgrowth of one or both condyles of the femur, so

Duration of Traumatic Change in Knee Following Injection of Dye into Traumatized and Normal Joints

Dye Used	Per Cent	Days	Dye Used	Per Cent	Days
Eosin	*0.025	39	Trypan blue	0.2	28
	0.02	28		0.5	35
	0.05	51	Neutral red	0.1	33
	*0.05	39		2	At once
	0.1	51			
	0.1	33	Janus green	0.2	39
	0.5	34	Safranin O	1	48
	2	40	Alum carmine	1	48
	2	At once			
Mercurochrome	0.05	35	Alizarin	Saturated solution	41
Isamine blue	1	40	Aniline blue	0.1	41

* Injections were made into the normal hip joints.

that laterally or medially they projected as large, irregular, bony masses. This condition was present only in the severer cases. In many cases there was an irregular, linear, osteophytic overgrowth of the ridges bordering the upper part of the intercondyloid fossa. In a few cases, defects in the tibial condylar cartilage were present, though more often a tear in the semilunar cartilage was noted. In only one case was a pedicled cartilaginous foreign body present. This is in accord with the experience of Moulonguet,[7] who noted that traumatic, experimentally detached, cartilaginous bodies were resorbed, unless pedicled.

The circumstances, then, are possibly not favorable for a selective staining of cartilage, as previously described in areas of natural arthritic erosion in cadavers. Fresh fractures in cartilage surely do not stain selectively. In no case, and with no dye used, was there a selective staining of these artificial areas of cartilaginous defect. In a few cases is was not possible to inject the dye into the joint, but in all joints in

7. Moulonguet, P.: Foreign Bodies in Joints, J. Bone & Joint Surg. **11**:353, 1929.

which the dye was present, uniform staining of cartilage resulted, depending on the strength of the solution of dye used. In this respect, the behavior of eosin and mercurochrome is interesting. Two things were noted previously about eosin: (*a*) it did not stain normal cartilage and (b) it was a selective stain for naturally diseased areas in cartilage, especially erosions (in cadavers). Eosin and mercurochrome are considered together because of their intimate relation to each other. Both, be it noted, stain normal cartilage in solutions that are above 0.05 per cent; at that level or below, cartilage is not stained, but synovia is. Our dilutions previously used were not so accurate. This is true of other dyes, the intensity of staining depending on the strength of the solution of the dye. Neither eosin nor mercurochrome, however, showed any selectivity for artificially traumatized areas in cartilage, as produced here. This, of course, does not mean that eosin does not stain selectively; we have seen it do so. It only means that under certain conditions, and our experience is as yet too limited to define those conditions, eosin does stain selectively. This demands more extensive investigation.

Neutral red, previously indicated as possibly selective in action, stained cartilage uniformly in strengths above 0.1 per cent; there was no selectivity. Alum carmine stained uniformly. Trypan blue, as noted by Menkin,[8] is fixed by inflammatory areas, when injected directly into them or intravenously; it is not fixed when injected at the periphery of such an area of inflammation. When injected intra-articularly, it stained uniformly and not selectively. This type of injection, then, possibly corresponds to a peripheral injection.

It should be noted that areas of erosion took up the dye, but no more so than did normal cartilage. No immediate reaction of the joints to dyes was noted. No metachromasia was present, except possibly in the case of Janus green, in which the color gamut of the stained cartilage ran from violet to blue.

SUMMARY

The injection of various dyes into normal joints and into joints experimentally traumatized produces an immediate, uniform, superficial staining of the cartilage of the joint. The artificially diseased areas in cartilage do not take up the stain selectively. No ill effect in the joints from the injection of dye in solutions of the strengths used was noted. If the dye is permitted to remain in the joint, it is absorbed, usually within a week.

8. Menkin, V.: An Aspect of Inflammation in Relation to Immunity, Arch. Path. **12**:802 (Nov.) 1931; Studies on Inflammation: VI. Fixation of Trypan Blue in Inflamed Areas of Frogs, J. Exper. Med. **53**:179, 1931.

FIFTY-FIRST REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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CONGENITAL ABNORMALITIES

Amniotic Origin of Deformities of the Limbs.—Hellner [1] studied a series of congenital malformations and amputations. He concluded that while amniotic bands could have been the cause of some of the deformities, defects in the mesenchymal tissue had to be considered as a cause in others. Absence of limbs could be produced experimentally by intra-uterine ligation of the limbs of embryos. To accomplish this it was found necessary to interrupt the circulation completely. Fractures in utero healed much as in extra-uterine life. While fibrous union of fractures was observed in a few instances, its frequency did not seem unusual to the observers.

Congenital Paramyotonia.—Urechia and his co-workers [2] reported a case of paramyotonia. This disease was characterized by rigid contractures of one or more limbs excited by temperature changes or other

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This report of progress is based on a review of 179 articles selected from 265 titles dealing with orthopedic surgery appearing in the various medical journals approximately between Nov. 26, 1932, and March 20, 1933. Only the publications which seemed to represent progress have been selected for review.

1. Hellner, Hans: Arch. f. klin. Chir. **172**:133, 1932.

2. Urechia, C. I.; Retezeanu, A., and Dragomir, L.: Bull. et mém. Soc. méd. d. hôp. de Paris **48**:1430, 1932.

stimuli. These contractures lasted from a few minutes to several hours and were followed by a flaccid paralysis lasting several hours. There was no true tetany. The patient was a girl of 15 whose grandmother had suffered from the same disease for twenty years. The girl had been normal until 4 years of age, since which time she had developed very slowly. She complained of painful cramps in both upper and lower limbs, lasting from one-half to two hours, followed by a feeling of weakness in the affected limb. There were no reflex or sensory changes present. Blood calcium was determined during and between attacks and was found to be 6 mg. per hundred cubic centimeters. Accordingly, parathyroid extract was administered daily for a week. The cramps persisted but were not so severe, and the blood calcium rose to 7.5 mg. per hundred cubic centimeters. After another week the blood calcium reached normal, and the cramps disappeared. No treatment was then given for ten days, at the end of which time the blood calcium had fallen to 7 mg. per hundred cubic centimeters, and the cramps returned. Treatment was therefore kept up at regular intervals. Coincidentally with this treatment, the patient grew very rapidly, put on weight and began to menstruate. The authors also reported the case of another patient in whose family paramyotonia had been present for four generations.

The Hip Joint from a Roentgenologic Standpoint.—Morrison [3] made a complete study of the development, from birth, of the epiphyses concerned in the formation of the component parts of the hip joint. Of greatest significance was his description of the anterior, superior and posterosuperior epiphyses of the acetabulum. He pointed out that the Y cartilage between the iliac, pubic and ischial portions of the acetabulum was a genetic center and grew in such a manner that it controlled the final width of the acetabulum. On the other hand, the superior three acetabular epiphyses controlled the depth of the acetabulum. The latter epiphyses appeared at about 12 years of age and fused with the acetabulum between the sixteenth and eighteenth years. Failure of fusion of these epiphyses resulted in the frequently seen ossicles in this area. Failure of development or absence of these superior acetabular epiphyses were held to be the etiologic factor in congenital dislocation of the hip. Following early reduction of congenital dislocation of the hip, if these epiphyses were absent, the acetabulum failed to deepen and redislocation occurred.

[ED. NOTE.—The studies of Morrison afford an interesting contrast to the views of Calot, who believes that a subluxation of the femoral head is the cause of the shallow acetabulum. Evidence may be adduced for both views.]

3. Morrison, L. B.: Am. J. Roentgenol. **28**:484, 1932.

DISTURBANCES IN OSSEOUS METABOLISM

Magnesium Rickets.—Meyer zu Hörste,[4] in experimental work with rats, found that a marked increase in the magnesium of the diet produced rickets of the same pathologic picture as that produced with diets poor in calcium, when a diet low in phosphate was used. He reviewed the literature in which it was observed that there was an increase in the magnesium content of bone in rickets and in osteomalacia. The author expressed the belief that the magnesium hindered the process of calcification in bone.

New Treatment for Rickets.—Bloom[5] reported that the addition of secondary calcium phosphate to the diet of children could prevent and cure rickets without the aid of vitamin D.

[ED. NOTE.—This abstract is given because it represents a radical departure from previous hypotheses concerning the etiology of rickets. A need of substantiation of the author's findings seems indicated.]

Changes in Bone and Photoviosterol Toxicosis.—Gottche and Kellner[6] studied the osseous changes in rats in intoxication due to viosterol. Osseous changes were observed in 19 of 106 rats which were given large doses of viosterol. In only 7 were the changes demonstrable by roentgenograms. The authors found that the osseous system was involved late, the order of frequency of involvement in this series being kidneys, aorta, stomach, lungs, muscles, glands of internal secretion and lastly bones. The bones showed gradually increasing atrophy. Microscopic examination showed the porosis of the cortex and trabeculae seen in the roentgenogram. There was narrowing of the epiphyseal cartilage bone. Porosis of the bone plus osteoid formation was the outstanding change. A summary of the literature was given.

Osteomalacia.—Wilson[7] investigated the treatment of osteomalacia (late rickets) by the daily administration of 1 drachm (3.75 cc.) of precipitated tricalcium phosphate. It was found that if the patients were able to walk about or work in the sunlight, healing took place in six weeks. If they were crippled and could only sit in the sunlight, there was no improvement. If they were kept indoors and deprived of both sunlight and adequate diet, whether they were crippled or could walk, almost no healing took place until vitamin D was given. It was suggested that muscular and circulatory activity in addition to sunlight could bring about an action similar to that of vitamin D.

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4. Meyer zu Hörste, G.: Klin. Wchnschr. **11**:1796, 1932.
5. Bloom, C. J.: South. M. J. **25**:1109, 1932
6. Gottche, O., and Kellner, B.: Arch. f. Kinderh. **97**:76, 1932.
7. Wilson, D. C.: Indian J. M. Research **20**:387, 1932.

Treatment of Osteomalacia with Viosterol: Decourt and Kaplan [8] believed that osteomalacia was not recognized as a rule until the bony changes and symptoms were so pronounced that the diagnosis was obvious. Early cases in which there were no symptoms and in which bony changes were not evident were manifested in a general physical asthenia without the cause being suspected. The disease could exist in a quiescent or abortive state. The good results following the use of viosterol in rickets led the authors to try it in cases of osteomalacia. They claimed no priority for this treatment but quoted from other authors who had tried the drug with success. The writers concluded that although osteomalacia responded well to viosterol, the disease could not be regarded as a simple avitaminosis. The need of vitamin D was thought to be associated with an endocrine disturbance of some sort.

Osseous Dystrophy Following Icterus Gravis Neonatorum.—Braid [9] described a case of a child who had icterus gravis neonatorum for several months, and who, between the second and third years, was found to have cystic conditions in the long bones. These abnormalities were limited to the diaphyses, and presented the same roentgenographic appearances under various forms of treatment during the subsequent years. Similar appearances had been noted in the long bones of puppies which had had their bile ducts occluded experimentally. Braid suggested that the explanation did not lie in the fact that the fat and calcium were less readily absorbed from the intestine in the absence of bile, but rather in that the retention of bile had impaired the functional capacity of the liver. He considered that possibly the liver is responsible for the distribution of vitamins A and D, which are so important in normal ossification.

NEOPLASMS

Hemangioma of a Vertebra.—Ireland [10] reported a case of hemangioma of a vertebra and gave summaries of 13 cases previously reported in the literature. He noted that 393 cases of hemangioma of a vertebra had been discovered at necropsy and had not given clinical symptoms. In all, the symptoms were insidious in onset, and were chiefly weakness, ataxia and spasticity. Pain was not an outstanding symptom. There was usually tenderness over the involved vertebra. The lesion was usually confined to a single vertebra, and the disk was not involved. The lower thoracic or lumbar vertebrae were usually affected. The diagnosis was made chiefly by roentgenogram. Differential diagnosis

8. Decourt, J., and Kaplan, S.: Paris méd. **2**:485, 1932.
9. Braid, F.: Arch. Dis. Childhood **7**:313, 1932.
10. Ireland, J.: Am. J. Roentgenol. **28**:372, 1932.

was often difficult. Treatment of the hemangiomas had consisted of roentgen therapy or application of radium; the latter was preferred by the author.

Benign Angiomatous Tumors of the Skeletal Muscles.—Two hundred and fifty-six reported cases of benign angiomatous tumors of the skeletal muscle were reviewed by Jenkins and Delaney,[11] and 62 of them were summarized in tabular form. Such tumors were found to occur in the first half of life and usually before 20 years of age. The etiology was not established. The usual symptoms were a slowly growing mass in the muscle tissue accompanied by a varying amount of pain, tenderness and functional disability. The tumor occurred most frequently in the extremities, especially the thighs. It was found to be diffuse more often than circumscribed. Operative removal was therefore extremely sanguineous and sometimes seriously so. Diagnosis was seldom made before operation. Findings pointing to a correct diagnosis were the recovery of blood by aspiration and the presence of phleboliths on roentgen examination. Microscopically, the tumors were found to have a cavernous structure filled with normal blood. Arteries, veins and capillaries were frequently present. In the stroma of connective tissue degenerative fibers of skeletal muscle were encountered, and this degenerative process was usually complete in the center of the tumor. Prognosis after surgical removal was found to be good. No deaths were reported. Incomplete removal of the tumor resulted in recurrence in several cases.

Malignant Giant Cell Tumor of Bone.—Methods of differentiating between benign and malignant giant cell tumors of bone were discussed by King,[12] and a report of a case of the malignant variety was given in detail. The typical histologic appearance of the malignant tumor was that of a very cellular stroma comprised chiefly of spindle cells with active nuclei and occasional mitotic figures. Tumor giant cells might not be present. If, however, in such a tissue infection, bone destruction or hemorrhagic degeneration occurred, the local picture changed, showing foreign giant cells and a pleomorphic stroma, both strongly suggestive of the innocent tumor. It was therefore obvious that if a portion was taken for histologic examinations it had to be removed from an area where no inflammatory or degenerative process was present. A very thorough examination had to be made of several sections, and the most valuable criterion of malignancy was taken to be the presence of mitotic figures. Roentgenographically, in the malignant variety, involvement of the cortex was seen and later a growth into the soft tissues.

11. Jenkins, H. P., and Delaney, P. A.: Surg., Gynec. & Obst. **55**:464, 1932.
12. King, E. S. J.: Brit. J. Surg. **20**:269, 1932.

Diagnosis of Diffuse Endothelial Myeloma.—Clopton and Womack [13] discussed the diagnosis of diffuse endothelial myeloma (Ewing's sarcoma). They considered the use of roentgen therapy the best method of diagnosis in doubtful cases. They stated that the cells of diffuse endothelial myeloma were extremely radiosensitive and that the tumor disappeared rapidly under this form of therapy. The authors reported in detail the cases of 5 patients suffering from this type of tumor.

[ED. NOTE.—General experience suggests that although roentgen therapy may cure the local condition, in most cases similar tumors develop elsewhere in the body and usually prove fatal.]

Sarcoma in Relation to Osteitis Deformans and Osteodystrophia Fibrosa.—Wanke [14] reported a case in detail and reviewed a number from the literature in which osteitis deformans had led to sarcomatous degeneration. From his observations he concluded that sarcoma developed only in a certain clinical type of osteitis deformans. In his case there were numerous small calcified nodules in the shaft of the femur in which the sarcoma later developed. Six similar cases with multiple development of sarcoma were found recorded in the literature. As further proof of a special presarcomatous type of osteitis deformans, the author mentioned the rarity of sarcoma in osteitis deformans (Speiser, 2.7 per cent; Codman, 14 per cent; Schmorl concluded that about 3 per cent of all persons over 40 showed some signs of osteitis deformans). Primary sarcoma might show a roentgen picture suggesting osteitis deformans and a marginal reaction histologically similar to osteitis deformans but with clinical signs of malignancy.

Diagnosis of Primary Tumors of Bone by Means of Roentgen Rays.—Moore,[15] in discussing the diagnosis of primary tumors of bone, stated that the best single factor in diagnosis was a series of good roentgenograms. It was best to regard tumors, when malignancy was in question, provisionally as sarcomas. These should be treated with intensive roentgen therapy while the diagnosis was being established. In giant cell tumors, roentgen therapy increased the symptoms, and this was followed by cure of the tumor. In osteogenic sarcoma, such treatment gave the best chance of cure while the neoplasm was being studied. Rapid improvement followed radiation of Ewing's sarcoma. In benign tumors, roentgen therapy prevented malignant change. Operation or biopsy was to be undertaken only when there was a reasonable certainty of the diagnosis.

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13. Clopton, W. B., and Womack, N. A.: Am. J. Cancer **16**:1444, 1932.
14. Wanke, R.: Deutsche Ztschr. f. Chir. **237**:198, 1932.
15. Moore, C.: M. Ann. District of Columbia **1**:285, 1932.

Neoplasms of the Os Calcis.—Coley and Sharp [16] reported a study of 32 neoplasms in the os calcis. Twenty-two of the tumors were found in men and 10 in women. The authors found that they occurred with about equal frequency at any age period. There were 13 osteogenic sarcomas, 10 endothelial myelomas and 9 giant cell tumors. The chief symptoms observed were pain and swelling about the ankle. For treatment, they advised the avoidance of weight-bearing. If the tumor proved to be an osteogenic sarcoma and no metastases were demonstrable, amputation was the best treatment. In endothelial myeloma, irradiation with the x-rays and the administration of erysipelas and prodigiosus toxins (Coley) resulted in cure. In giant cell tumors, curettage followed by radiation was advocated.

Osteoplastic Metastases in Prostatic Carcinoma.—Cave [17] described extensive metastases to bones originating from an adenocarcinoma of the prostate. Roentgenographically, the metastatic area was more dense, and chemically the bones involved were found to contain 44 per cent more mineral content than the normal. The proportion of calcium carbonate was also found to be greatly increased. It was pointed out that the carbonate was more opaque to roentgen rays than the phosphate. Metastases to bone were stated to have occurred in 70 per cent of cases of prostatic carcinoma. The method of spread was discussed.

Metastatic Malignant Lesions in Bones.—Sutherland and his co-workers [18] reviewed 1,032 cases of metastatic lesions in bones observed at the Mayo Clinic. They believed that the spread of the tumor to the bones was usually by the lymphatics, but in certain cases the blood stream was the only possible route. The degree of malignancy of the primary tumor determined chiefly the extent of the metastases. The tumor which produced osseous metastases most frequently was carcinoma of the breast. These metastases were chiefly of the osteoclastic type. The portions of the skeleton usually involved were the lumbar spine, the pelvis, the femora and the ribs. Carcinoma of the prostate was second in the frequency in which it was followed by osseous metastases. The metastatic tumors were often found before any pathologic change in the prostate had been suspected. These tumors were usually osteoplastic, and they were commonly found in the spinal column, pelvis and femur. Metastatic tumors in bone were frequently observed from hypernephroma and carcinoma of the bladder, and these tumors were usually osteoclastic in type. In carcinoma of the thyroid gland, metastatic tumors were seen rarely before the age of 50. Carcinoma of the lung often

16. Coley, B. L., and Sharp, G. S.: Am. J. Cancer **16**:1053, 1932.

17. Cave, P.: Brit. J. Radiol. **5**:745, 1932.

18. Sutherland, C. G.; Decker, F. H., and Cilley, E. I. L.: Am. J. Cancer **16**:1457, 1932.

had a metastatic tumor only in one vertebral body. In carcinoma of the cervix and ovary, metastatic tumors in bone were observed only in about 2 per cent of the cases. Osseous metastases were rare in carcinoma of the stomach and in melano-epithelioma. In abdominal carcinoma, metastases were not common. When they occurred, they were usually osteoclastic. In carcinoma of the colon, osseous metastases were usually found in the spine. Metastatic tumors of any kind observed in the spine were usually central in origin. In the vertebral body there was no involvement of the disk, evidence of bony proliferation or enlargement of the vertebra.

Bone Metastases from Carcinoma of the Breast.—In a study of 106 cases of cancer of the breast, Downs[19] found osseous metastases in 33 per cent. The occurrence given in the literature varied from 5 to 53 per cent. The bones most frequently involved were the femora, pelvis, ribs, lumbar spine and skull, in the order given. The average time between the recognition of the tumor and the discovery of metastases in bone was four years and eight months. Of 57 patients with metastases, visceral as well as osseous, 44 were dead. A study of pathologic material did not confirm the statement by Copeland that most mammary carcinoma with metastases to bone was scirrhous. Scirrhous carcinoma was found in only 33 per cent of the cases with metastases to bone.

POLIOMYELITIS

Drinker Respirator in the After-Cure of Infantile Paralysis.—Legg[20] reported his observations on the use of the Drinker respirator in cases of infantile paralysis treated by the Harvard Infantile Paralysis Commission. He used it not only during the acute stage of the disease as a life-saving measure, but also later as a passive exerciser of the muscles of respiration. Measurements of voluntary expansion of the chest taken on a series of patients who received regular daily treatment in the respiration machine over a period of months showed a definite and steady increase from amounts under ½ inch (1.27 cm.) up to 2 and 3 inches (5 and 7.6 cm.) of voluntary expansion away from the machine. Consequently, the extreme deformities of the chest commonly observed in extensive paralysis were for the most part prevented.

Drinker Respirator in Respiratory Failure in Poliomyelitis.—Wesselhoeft and Smith[21] reviewed 30 cases of respiratory failure following infantile paralysis in which the Drinker respirator was used. Thirteen of the 30 patients survived owing, in the authors' opinion, wholly to the

19. Downs, E. E.: J. M. Soc. New Jersey **29**:957, 1932.

20. Legg, T.: Use of the Drinker Respirator in After-Care of Infantile Paralysis, J. A. M. A. **100**:647 (March 4) 1933.

21. Wesselhoeft, C., and Smith, E. C.: New England J. Med. **207**:559, 1932.

use of the respirator. They noted a much better response in the cases of spinal respiratory paralysis than in those of bulbar type. They emphasized the importance of having satisfactory respiratory apparatus available during epidemics of infantile paralysis.

Neutralization Tests of Serums of Treated and Untreated Patients with Poliomyelitis.—A series of carefully controlled in vitro experiments were performed by Howitt [22] to determine whether convalescent poliomyelitic serum had a variable potency. The author concluded that patients showing a complete recovery after transient or only slight paralysis gave more evidence of the production of a potent serum than those in whom severe paralysis developed. Likewise, antiviral substances might be present in a certain percentage of treated persons, but those who received [14] antipoliomyelitic serum showed less tendency to produce neutralizing substances than untreated persons.

[ED. NOTE.—The results of these experiments may aid in explaining certain discrepancies in reports on the treatment of poliomyelitis with human convalescent serum. They suggest the need for giving serum from known tested donors who either have recovered from the disease or are naturally immune to it. The use of a standardized serum from immunized large animals would naturally be indicated.]

TUBERCULOSIS

Tuberculosis of the Bones and Joints in Children.—Hyde [23] reported that during the past ten years 4 per cent of all applicants to Springfield Lake Sanitarium, Ohio, have had definite tuberculosis of the bones or joints whereas 5 per cent of the 1,220 children among the applicants were so afflicted. Thirty-nine per cent of the cases originated before the sixth year, and 57 per cent before the sixteenth year. Tuberculosis of the bones and joints was usually the result of metastases from disease in the lungs or lymph nodes. The metastases were often blood-borne, and multiple lesions involving various organs or tissues might develop. An average of 2.6 tuberculosis lesions per patient was found in this group. The site of metastasis was favored by injury and local disturbances of nutrition. Twenty-seven per cent of adults and children gave a history of injury. The average duration of the disease in this series of children, including all types of bone and joint lesions, was about five years. The author felt that this period could have been shortened practically one-half had earlier diagnosis been made, adequate treatment given and unwise surgical intervention been omitted. Conservative treatment was the method of choice for children: "orthopedic

22. Howitt, B. F.: J. Infect. Dis. **51**:565, 1932
23. Hyde, C. L.: Am. Rev. Tuberc. **26**:625, 1932.

rest, adequate diet, heliotherapy and open air life," the first two therapeutic procedures being of greatest importance. Surgical measures were not to be considered until the disease had become quiescent or arrested.

[ED. NOTE.—This excellent article merits careful reading and consideration. Emphasis placed on the general care of the tuberculous bones or joints to the exclusion of a single method of therapy is the only accepted method of treatment. Early operative therapy is often followed by disaster.]

Positive Pressure in Arthrodesis for Tuberculosis of the Knee Joint.—Key [24] observed that a certain number of tuberculous knee joints failed to obtain bony ankylosis in spite of complete excision and prolonged immobilization. To secure ankylosis more surely, he devised a method of maintaining positive pressure between the excised ends of bone. A Steinman pin was inserted through the lower end of the femur and another through the upper end of the tibia. The pins were connected by turnbuckle screws. Immobilization was secured by a plaster cast from toes to groin. Constant pressure was maintained by the turnbuckle screws. Bony union was usually found in eight weeks. Unprotected weight-bearing was permitted in sixteen weeks.

24. Key, J. A.: South. M. J. **25**:909, 1932.

(To be continued)

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